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SRV Biology Part 3

Brainard **Gray-Wilson** **Wilkin**

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Chapter 1

Nervous and Endocrine Systems

1.1 The Nervous System

Lesson Objectives

- Identify the type of cells that make up nervous tissue.
- Describe the structure of a neuron.
- Relate membrane potential to action potential.
- Outline the role of neurotransmitters in neuron communication.
- Distinguish between the sensory and motor divisions of the peripheral nervous system.
- Describe the structure of the eye and identify the roles of rods and cones in vision.
- Describe the structure of the ear and identify the structures that are important to hearing and balance.
- Distinguish between the receptors for pain, pressure, and temperature.
- Identify the main effect of psychoactive drugs on the CNS.
- Summarize the mechanism of addiction.

Introduction

Your body has two systems that help you maintain homeostasis: the nervous system and the endocrine system. The **nervous system** is a complex network of nervous tissue that sends electrical and chemical signals. The nervous system includes the central nervous system (CNS) and the peripheral nervous system (PNS) together. The **central nervous system** is made up of the brain and spinal cord, and the **peripheral nervous system** is made up of the nervous tissue that lies outside the CNS, such as the nerves in the legs, arms, hands, feet and organs of the body. The nervous system mediates communication between different parts of the body as well as the body's interactions with the environment.

The **endocrine system** is a system of glands around the body that release chemical signal molecules into the bloodstream. The electrical signals of the nervous system move very rapidly along nervous tissue, while the chemical signals of the endocrine system act slowly in comparison and over a longer period of time. Working together, the nervous and endocrine systems allow your body to respond to short or long term changes in your environment, such as a pedestrian suddenly stepping out in front of your bike, or your body adapting to cycling in a warm, humid summer evening, as shown in **Figure** 1.1.

Figure 1.1: Cycling home in rush-hour traffic demands a lot of your nervous and endocrine systems. Your nervous system

Nerve Cells

Although the nervous system is very complex, there are only two main types of nerve cells in nervous tissue. All parts of the nervous system are made of nervous tissue. The **neuron** is the ”conducting” cell that transmits electrical signals, and it is the structural unit of the nervous system. The other type of cell is a glial cell. **Glial cells** provide a support system for the neurons, and recent research has discovered they are involved in synapse formation. A type of glial cell in the brain, called **astrocytes**, is important for the maturation of neurons and may be involved in repairing damaged nervous tissue. Neurons and glial cells make up most of the brain, the spinal cord and the nerves that branch out to every part of the body. Both neurons and glial cells are sometimes referred to as nerve cells.

Structure of a Neuron

The special shape of a neuron allows it to pass an electrical signal to another neuron, and to other cells. Electrical signals move rapidly along neurons so that they can quickly pass “messages” from one part of the body to another. These electrical signals are called nerve impulses.

Neurons are typically made up of a cell body (or soma), dendrites, and an axon, as shown in **Figure** 1.2. The cell body contains the nucleus and other organelles similar to other body cells. The **dendrites** extend from the cell body and receive a nerve impulse from another cell. The cell body collects information from the dendrites and passes it along to the axon. The **axon** is a long, membrane-bound extension of the cell body that passes the nerve impulse onto the next cell. The end of the axon is called the **axon terminal**. The axon terminal is the point at which the neuron communicates with the next cell. You can say the dendrites of the neuron receive the information, the cell body gathers it, and the axons pass the information onto another cell.

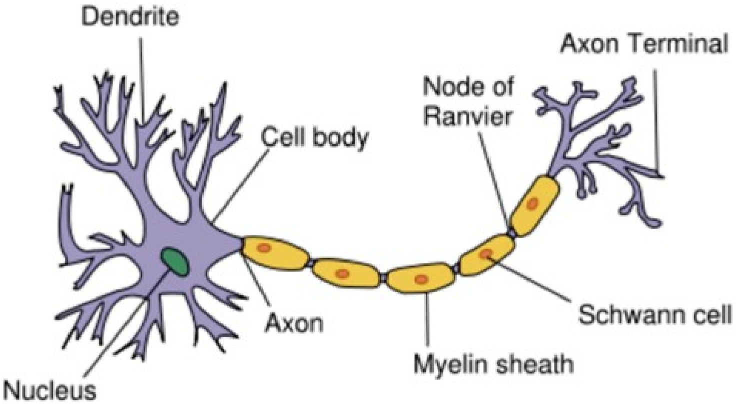

Figure 1.2: The general structure of a neuron. Neurons come in many different shapes and sizes, but they all have a cell body, dendrites, and an axon. The cell body contains a nucleus and other organelles. However, not all neurons have a myelin sheath.

The axons of many neurons are covered with an electrically insulating phospholipid layer called a **myelin sheath**. The myelin speeds up the transmission of a nerve impulse along the axon. It acts like a layer of insulation, like the plastic you would see around an electrical cord.

The myelin is an outgrowth of glial cells. **Schwann cells** which are shown wrapped around the neuron in **Figure** 1.2, are a type of glial cell. Schwann cells are flat and thin, and like other cells, contain a nucleus and other organelles. Schwann cells supply the myelin for neurons that are not part of the brain or spinal cord, while another type of glial cell, called **oligodendrocytes**, supply myelin to those of the brain and spinal cord. Myelinated neurons are white in appearance, and they are what makes up the ”white matter” of the brain. A cross section of a myelinated neuron is shown in **Figure** 1.3. Myelin is not continuous along the axon. The regularly spaced gaps between the myelin are called **Nodes of Ranvier**. The nodes are the only points at which ions can move across the axon membrane, through ion channels. In this way the nodes act to strengthen the nerve impulse by concentrating the flow of ions at the nodes of Ranvier along the axon.

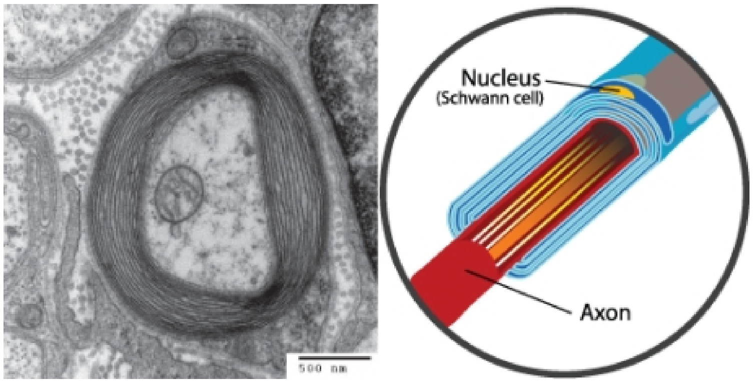

Figure 1.3: A transmission electron microscope (TEM), image of a cross section of a myelinated axon. The

Neurons are specialized for the passing of cell signals. Given the many functions carried out by neurons in different parts of the nervous system, there are many different of shapes and sizes of neurons. For example, the cell body of a neuron can vary from 4 to 100 micrometers in diameter. Some neurons can have over 1,000 dendrite branches, which make connections with tens of thousands of other cells. Other neurons have only 1 or 2 dendrites, each of which has thousands of synapses. A **synapse** is a specialized junction at which neurons communicate with each other, and is shown in **Figure** 1.4. Also, a neuron may have 1 or many axons. The longest axon of a human motor neuron can be over a meter long, reaching from the base of the spine to the toes. Sensory neurons have axons that run from the toes to the spinal cord, over 1.5 meters in adults. Giraffes have single axons several meters in length running along the entire length of their necks.

Nerve Impulses

In the late 18th century, the Italian doctor and physicist Luigi Galvani first recorded the action of electricity on the muscle tissue of frogs. He noted that an electrical charge applied to a nerve in the legs of a dead frog made the legs move. Galvani attributed the movement of the frog's muscles to an electrical current that was carried by the nerves. Galvani coined the term "animal electricity" to describe this vital force for life.

Galvani believed that animal electricity came from the muscle and was unique to living creatures. However, his fellow Italian, and physicist, Alessandro Volta disagreed with him and reasoned that animal electricity was a physical phenomenon, that occurred between metals. Volta disproved Galvani's claim by building the first battery, which showed that a current could flow outside an organism's body. Since then scientists have learned much about electrical charges in living systems.

Ion Channels and Nerve Impulses

Ion transport proteins have a special role in the nervous systems because voltage-gated ion channels and ion pumps are essential for forming a nerve impulse. Ion channels use energy to build and maintain a concentration gradient of ions between the extracellular fluid and the cell's cytosol, as shown in **Figure**

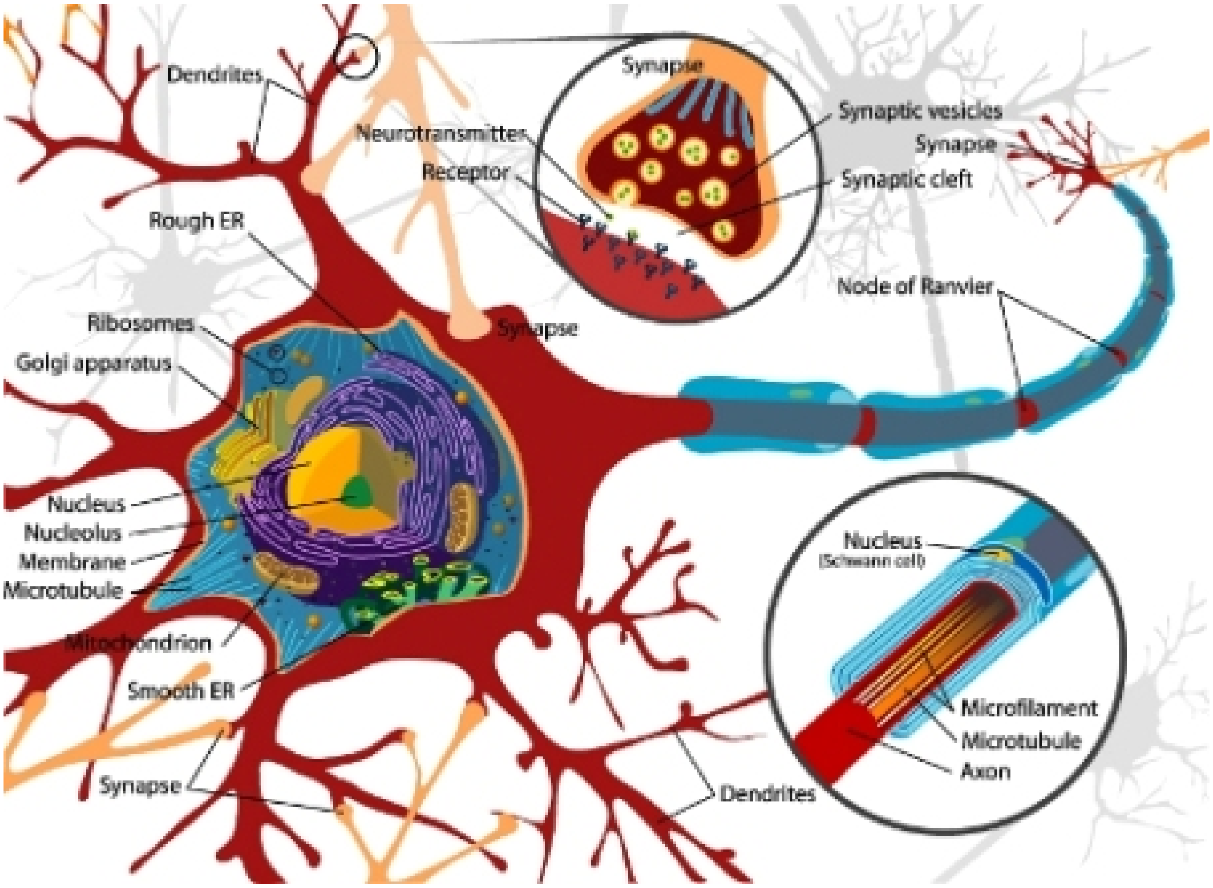

Figure 1.4: The location of synapses. Synapses are found at the end of the axons (called axon terminals) and help connect a single neuron to thousands of other neurons. Chemical messages called neurotransmitters are released at the synapse and pass the

1.5. This concentration gradient results in a net negative charge on the inside of the membrane and a positive charge on the outside. Ion channels and ion pumps are very specific; they allow only certain ions through the cell membrane. For example, potassium channels will allow only potassium ions through, and the **sodium-potassium pump** acts only on sodium and potassium ions.

All cells have an electrical charge which is due to the concentration gradient of ions that exists across the membrane. The number of positively charged ions outside the cell membrane is greater than the number of positively charged ions in the cytosol. This difference causes a voltage difference across the membrane. **Voltage** is electrical potential energy that is caused by a separation of opposite charges, in this case across the membrane. The voltage across a membrane is called **membrane potential**. Membrane potential is the basis for the conduction of nerve impulses along the cell membrane of neurons. Ions that are important in the formation of a nerve impulse include sodium (Na^+) and potassium (K^+).

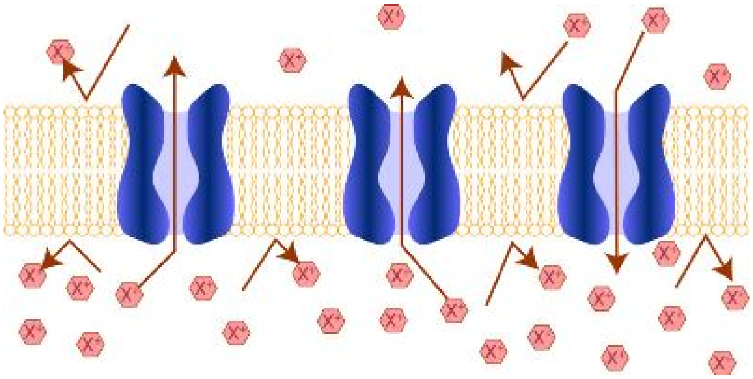

Figure 1.5: Channel proteins in the plasma membrane. Membrane channel proteins (or channel proteins), allow the movement of specific ions across the cell membrane, in this case the hypothetical

Resting Potential

When a neuron is not conducting a nerve impulse, it is said to be at rest. The **resting potential** is the resting state of the neuron, during which the neuron has an overall negative charge. In neurons the resting potential is approximately -70 milliVolts (mV). The negative sign indicates the negative charge inside the cell relative to the outside.

The reasons for the overall negative charge of the cell include:

- The sodium-potassium pump removes Na^+ ions from the cell by active transport. A net negative charge inside the cell is due to the higher concentration of Na^+ ions outside the cell than inside the cell.
- Most cells have potassium-selective ion channel proteins that remain open all the time. The K^+ ions move down the concentration gradient (passively) through these potassium channels and out of the cell, which results in a build-up of excess positive charge outside of the cell.
- There are a number of large, negatively charged molecules, such as proteins, inside the cell.

Action Potential

An **action potential** is an electrical charge that travels along the membrane of a neuron. It can be generated when a neuron's membrane potential is changed by chemical signals from a nearby cell. In an action potential, the cell membrane potential changes quickly from negative to positive as sodium ions flow into and potassium ions flow out of the cell through ion channels, as shown in **Figure** 1.6.

The change in membrane potential results in the cell becoming depolarized. An action potential works on an all-or-nothing basis. That is, the membrane potential has to reach a certain level of depolarization, called the **threshold**, otherwise an action potential will not start. This threshold potential varies, but is generally about 15 millivolts (mV) more positive than the cell's resting membrane potential. If a membrane depolarization does not reach the threshold level, an action potential will not happen. You can see in **Figure** 1.7 how two depolarizations did not reach the threshold level of -55mV. The first channels to open are the sodium ion-channels, which allow sodium ions to enter the cell. The resulting increase in positive charge inside the cell (up to about +40 mV) starts the action potential. Potassium ion-channels then open up, allowing potassium ions out of the cell, which ends the action potential. Both of the ion channels then close, and the sodium-potassium pump restores the resting potential of -70 mV. The action potential will move down the axon toward the synapse like a wave would move along the surface of water.

In myelinated neurons, ion flows occur only at the nodes of Ranvier. As a result, the action potential signal "jumps" along the axon membrane, from node to node, rather than spreading smoothly along the membrane, as they do in axons that do not have a myelin sheath. This is due to clustering of Na^+ and K^+ ion channels at the Nodes of Ranvier. Unmyelinated axons do not have Nodes of Ranvier; and ion channels in these axons are spread over the entire membrane surface.

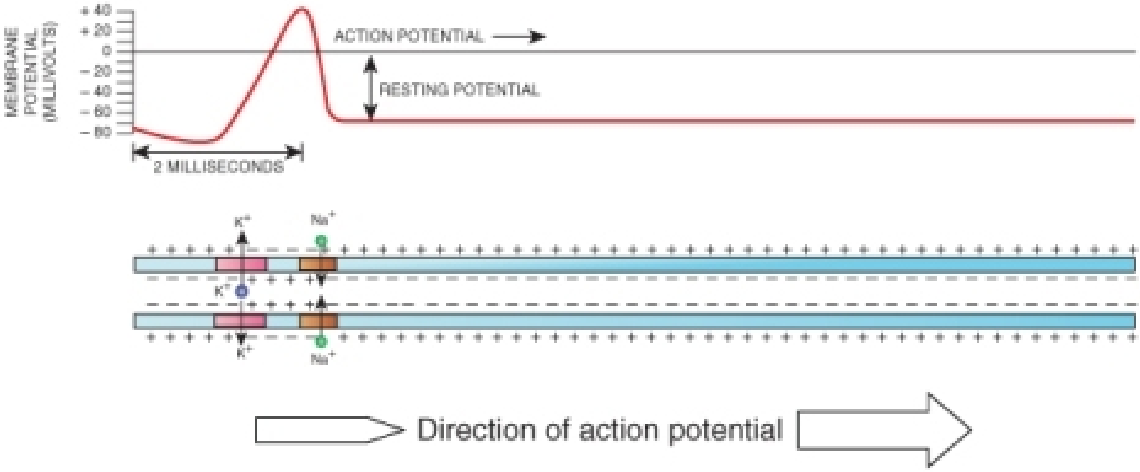

Figure 1.6: The movement of an action potential down an axon. A chemical message from another nerve causes the sodium ion channels at one point in the axon to open. Sodium ions rush across the membrane and cause the interior of the axon to become positively charged (depolarized) because the cell now contains more positive charges. Potassium ion channels then open and potassium ions flow out of the cell, which end the action potential. The action potential then moves down the axon membrane toward the synapse.

Types of Neurons

Neurons are highly specialized for the processing and transmission of cellular signals and can be classified by their structure or function. Structural classification is based on the number of dendrites and axons that a cell has. Functional classification groups neurons according to the direction in which the nerve impulse

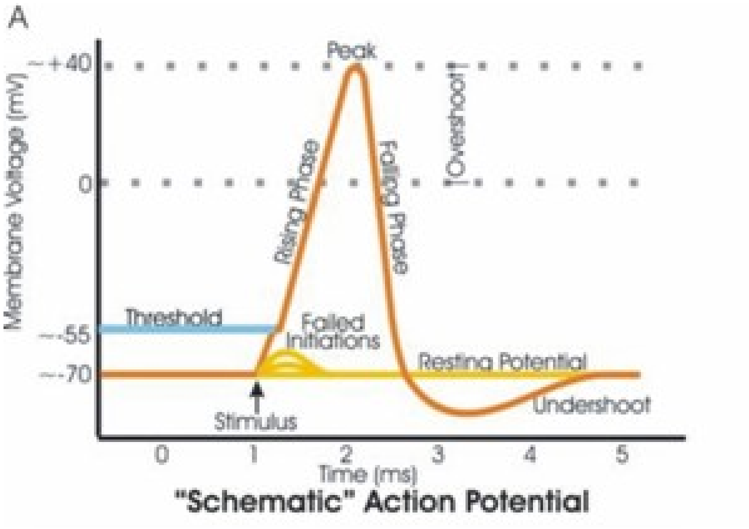

Figure 1.7: The changes in membrane potential during an action potential. Note the failed initiations that did not start an action potential. These depolarizations did not reach the threshold level (of about -55mV), so they did not start an action potential.

is moving in relation to the CNS.

We will discuss the three functional groups of nerves:

- **Sensory neurons** carry signals from tissues and organs to the central nervous system and are sometimes also called afferent neurons. Sensory neurons typically have a long dendrite and short axon. Sensory neurons are found in reflex arcs and are involved in several forms of involuntary behavior, including pain avoidance.
- **Motor neurons** carry signals from the central nervous system to muscles and glands and are sometimes called efferent neurons. Motor neurons have a long axon and short dendrites.
- **Interneurons** connect sensory and motor neurons in neural pathways that go through the central nervous system. Interneurons are also called association or relay neurons. Interneurons are found only in the central nervous system where they connect neuron to neuron.

Communication Between Neurons

Neurons communicate with each other at specialized junctions called synapses. Synapses are also found at junctions between neurons and other cells, such as muscle cells like the one shown in **Figure** 1.8. To see a synapse between two neurons, refer to **Figure** 1.4.

There are two types of synapses:

- **chemical synapses** use chemical signaling molecules as messengers
- **electrical synapses** use ions as messengers

We will primarily discuss chemical synapses in this chapter. The axon terminal of one neuron usually does not touch the other cell at a chemical synapse. Between the axon terminal and the receiving cell is a gap called a **synaptic cleft**. The transmitting cell is called the presynaptic neuron, and the receiving cell is called the postsynaptic cell or if it is another neuron, a postsynaptic neuron.

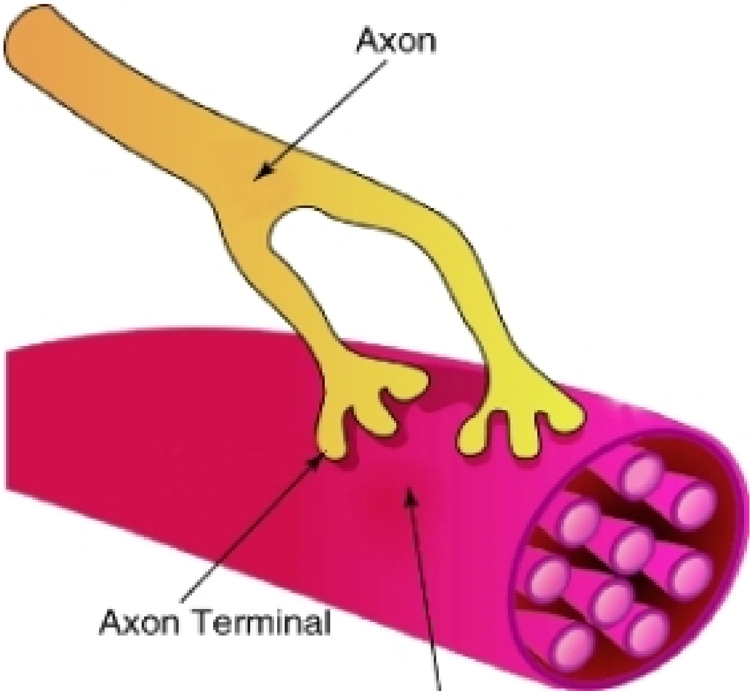

Figure 1.8: A synapse between a neuron and a muscle cell. The connection between a neuron and a muscle cell, called a

Your brain has a huge number of synapses. Each of your 10^{12} (one trillion) neurons—including glial cells—has on average 7,000 synaptic connections to other neurons. It has been estimated that the brain of a three-year-old child has about 10^{16} synapses (10 quadrillion). This number declines with age, and levels off by adulthood. An adult has between 10^{15} and 5 x 10^{15} synapses (1 to 5 quadrillion).

Neurotransmitter Release

When an action potential reaches the axon terminal, it causes the neurotransmitter vesicles to fuse with the terminal membrane, and the neurotransmitter is released into the synaptic cleft. A **neurotransmitter** is a chemical message that is used to relay electrical signals between a neuron and another cell. Neurotransmitter molecules are made inside the presynaptic neuron and stored in vesicles at the axon terminal. Some neurons make only one type of neurotransmitter, but most neurons make two or more types of neurotransmitters.

When an action potential reaches the axon terminal, it causes the neurotransmitter vesicles to fuse with the terminal membrane. Neurotransmitter is released into the synaptic cleft. The neurotransmitters then diffuse across the synaptic cleft and bind to receptor proteins on the membrane of the postsynaptic cell, as shown in **Figure** 1.9.

Animations of neurons and neurotransmitters: http://www.brainexplorer.org/neurological_control/Neurological_-Neurotransmission.shtml

Neurotransmitter Action

Many types of neurotransmitters exist, a few of which are listed in **Table** 1.1. Neurotransmitters can have an excitatory or inhibitory effect on the postsynaptic cell. An excitatory neurotransmitter initiates

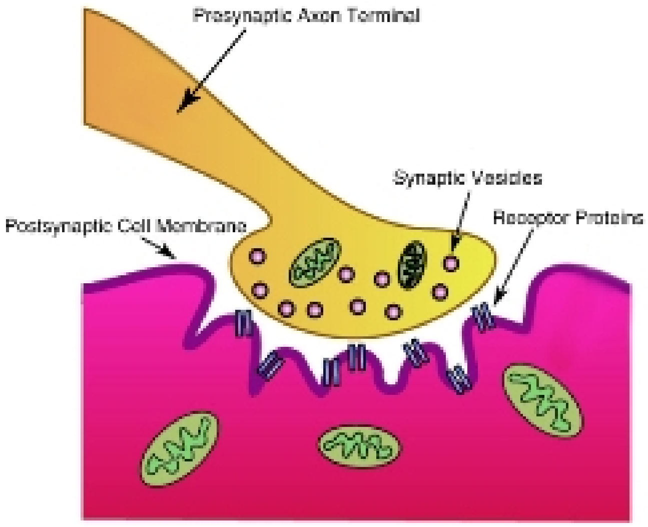

Figure 1.9: The synaptic cleft. Neurotransmitter that is released into the synaptic cleft diffuses across the synaptic membrane and binds to its receptor protein on the post synaptic cell.

an action potential and an inhibitory neurotransmitter prevents one from starting. Glutamate is the most common excitatory transmitter in the body while GABA and glycine are inhibitory neurotransmitters. The release of acetylcholine, an excitatory neurotransmitter causes an inflow of positively charged sodium ions (Na^+) into the postsynaptic neuron. This inflow of positive charge causes a depolarization of the membrane at that point. The depolarization then spreads to the rest of the postsynaptic neuron. Acetylcholine is the neurotransmitter that initiates muscle movement.

The effect of a neurotransmitter also can depend on the receptor it binds to. That is, a single neurotransmitter may be excitatory to the receiving neuron, or it may inhibit such an impulse by causing a change in the membrane potential of the cell. Synapses too can be excitatory or inhibitory and will either increase or decrease activity in the target neuron, based on the opening or closing of ion channels.

Table 1.1: **Common Neurotransmitters and Their Receptors**

Name	Receptor Name and Type	Ions Involved
Glutamate (glutamic acid)	Glutamate receptors (ligand-gated ion channels and G protein-coupled receptors)	Ca2+, K+, Na+
Acetylcholine	Acetylcholine receptors (ligand-gated ion channel)	Na+
Norepinephrine (noradrenaline)	Adrenoceptors (G protein-coupled receptors)	Ca2+
Epinephrine (adrenaline)	Adrenoceptors (G protein-coupled receptors)	Ca2+

Table 1.1: (continued)

Name	Receptor Name and Type	Ions Involved
Serotonin (5-hydroxytryptamine)	5-HT receptors 5-HT_3 is a ligand-gated ion channel 5-HT_1, 5-HT_2, 5-HT_4, $5\text{-HT}_5\text{A}$, 5-HT_7 are G protein-coupled receptors	K+, Na+
Gamma-aminobutyric acid (GABA)	GABA_A and GABA_C (ligand-gated ion channels) GABA_B (G protein-coupled receptors)	Cl- K+
Histamine	Histamine receptors (H1, H2, H3, H4) (G protein-coupled receptors)	

Neurotransmitter receptors can be gated ion channels that open or close through neurotransmitter binding or they can be protein-linked receptors. Protein-linked receptors are not ion channels; instead they cause a signal transduction that involves enzymes and other molecules (called second messengers) in the postsynaptic cell. Refer to the *Cell Structure and Function* chapter for more information about signal transduction mechanisms.

Neurotransmitter Reuptake

Many neurotransmitters are removed from the synaptic cleft by neurotransmitter transporters in a process called reuptake. **Reuptake** is the removal of a neurotransmitter from the synapse by the pre-synaptic neuron. Reuptake happens after the neurotransmitter has transmitted a nerve impulse. Without reuptake, the neurotransmitter molecules might continue to stimulate or inhibit an action potential in the post-synaptic neuron. The process of release and reuptake of neurotransmitters is shown in **Figure** 1.10.

Re-uptake is carried out by transporter proteins which bind to the released transmitter and actively transport it across the plasma membrane into the pre-synaptic neuron. The reuptake of neurotransmitter is the target of some types of medicine. For example, serotonin is a neurotransmitter that is produced by neurons in the brain. Serotonin is believed to play an important role in the regulation of mood, emotions, and appetite. After release into the synaptic cleft, serotonin molecules either attach to the serotonin receptors (called 5-HT receptors) of the post-synaptic neuron, or they attach to receptors on the surface of the presynaptic neuron that produced the serotonin molecules, for reuptake. Reuptake is a form of recycling because the neuron takes back the released neurotransmitter for later use. Medicines called selective serotonin reuptake inhibitors (SSRIs) block the reuptake of the neurotransmitter serotonin. This blocking action increases the amount of serotonin in the synaptic cleft, which prolongs the effect of the serotonin on the postsynaptic neuron. Some scientists hypothesize that decreased levels of serotonin in the brain are linked to clinical depression and other mental illnesses. So SSRI medications such as sertraline and fluoxetine are often prescribed for depression and anxiety disorders.

Another way that a neurotransmitter is removed from a synapse is digestion by an enzyme. At cholinergic synapses (where acetylcholine is the neurotransmitter), the enzyme acetylcholinesterase breaks down the acetylcholine.

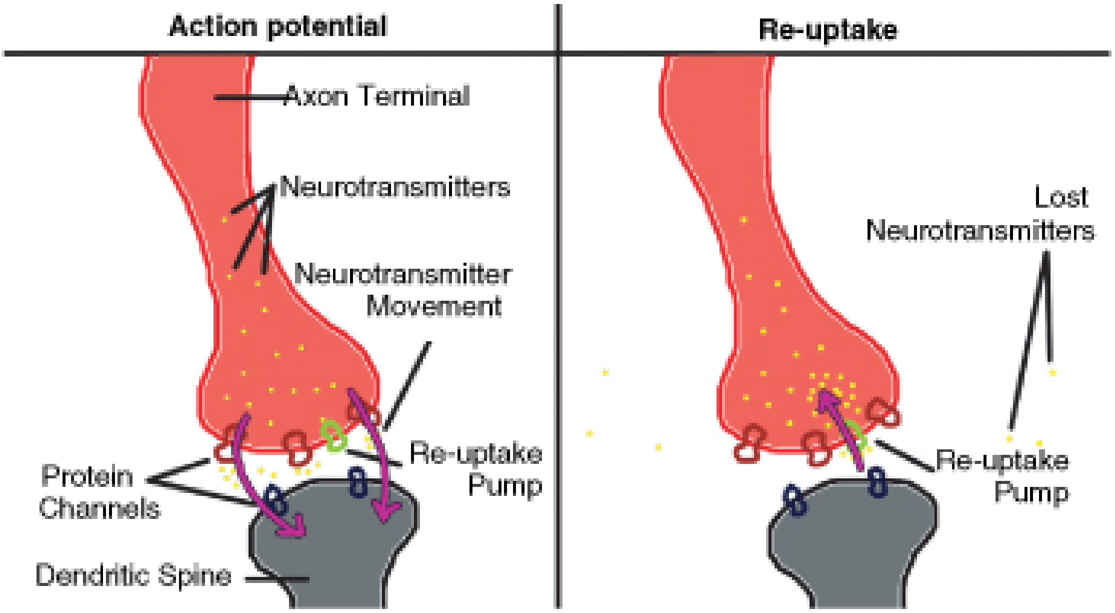

Figure 1.10: A synapse before and during reuptake. Neurotransmitter transporter proteins (also called reuptake pumps) release the neurotransmitter and also reuptake it from the synaptic cleft. Reuptake is a way of controlling the effect the neurotransmitter has on the post-synaptic cell.

Neurotransmitters and Disease

Diseases that affect nerve communication can have serious consequences. A person with Parkinson's disease has a deficiency of the neurotransmitter dopamine. Progressive death of brain cells that produce dopamine increases this deficit, which causes tremors, and a stiff, unstable posture. L-dopa is a chemical related to dopamine that when given as a medicine, eases some of the symptoms of Parkinson's disease. The L-dopa acts as a substitute neurotransmitter, but it cannot reverse the disease.

The soil bacterium *Clostridium tetani* produces a neurotoxin that causes the disease tetanus. The bacteria usually get into the body through an injury caused by an object that is contaminated with *C. tetani* spores, such as a puncture wound caused by stepping on a nail. The *C. tetani* neurotoxin blocks the release of the neurotransmitter GABA, which causes skeletal muscles to relax after contraction. When the release of GABA is blocked, the muscle tissue does not relax and remains contracted. Tetanus can be fatal when it affects the muscles used in breathing. Thankfully, tetanus is treatable and can be prevented by vaccination.

Another bacterium called *Clostridium botulinum* produces a toxin that is occasionally found in preserved foods that have been improperly sterilized. The toxin causes a disease called botulism. Botulin toxin blocks the release of the excitatory neurotransmitter acetylcholine. Blockage of acetylcholine causes the progressive relaxation of muscles because they are unable to contract. Paralysis of the muscles used for breathing can be fatal unless the patient is treated with a respirator.

More information on diseases: http://www.brainexplorer.org/neurological_control/Neurological_Disorders.shtml

Synapses and Recent Research

Recent studies have found that electrical synapses are more common in the central nervous system than were previously thought. An electrical synapse is a link between two neighboring neurons that is formed at a narrow gap between the pre- and postsynaptic cells called a **gap junction**. At gap junctions, cells are about 3.5 nm from each other, a much shorter distance than the 20 to 40 nm distance that separates cells at chemical synapses.

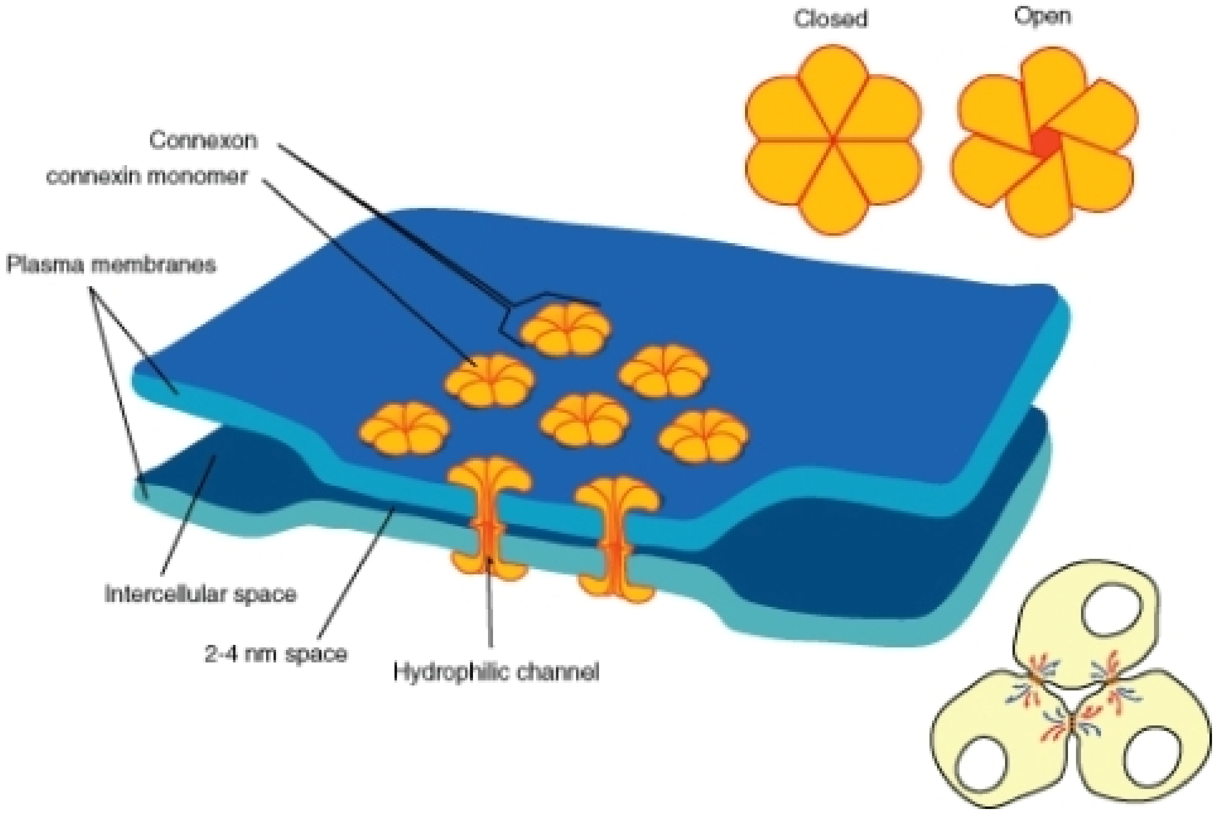

Figure 1.11: Electrical synapses. Electrical synapses are more common in the nervous system than was once thought. Cell signaling at electrical synapses is much faster than signaling at chemical synapses. The image at the bottom left of the figure shows the location of gap junctions between cells.

Each gap junction has many channels which cross the plasma membranes of both cells, as is shown in **Figure** 1.11. Gap junction channels are wide enough to allow ions and even medium sized molecules like signaling molecules to flow from one cell to the next. For example, when positive ions move through the channel into the next cell, the extra positive charges depolarize the postsynaptic cell.

Signaling at electrical synapses is faster than the chemical signaling that occurs across chemical synapses. Ions directly depolarize the cell without the need for receptors to recognize chemical messengers, which occurs at chemical synapses. Such fast communication between neurons may indicate that in some parts of the brain large groups of neurons can work as a single unit to process information. Electrical synapses are numerous in the retina and cerebral cortex.

In addition to neurons, glial cells are an important part of the nervous system. The word *glia* means "glue" in Greek. Glial cells can be thought of as partners to neurons by aiding in the maintenance of homeostasis, signal transduction, formation of myelin and providing support and nutrition. The importance of neurons as the conductive cells of the nervous system, known as the neuron doctrine, has been questioned by recent research. The role of glial cells in processing neural information has begun to be appreciated more. There are far more glial cells than neurons, it has been estimated that glial cells outnumber neurons by as many as 50:1.

Central Nervous System

The central nervous system (CNS), which includes the brain and the spinal cord, shown in **Figure** 1.12, represents the largest part of the nervous system. The brain is the central control of the nervous system. The spinal cord carries nerve impulses from the brain to the body and from the body to the brain. Together with the peripheral nervous system (PNS), which includes all nervous tissue outside of the central nervous system, it controls virtually every activity in the body. The brain is protected by the skull and the spinal cord is protected by the vertebrae. An overview of the CNS can be viewed at http://vimeo.com/2024719.

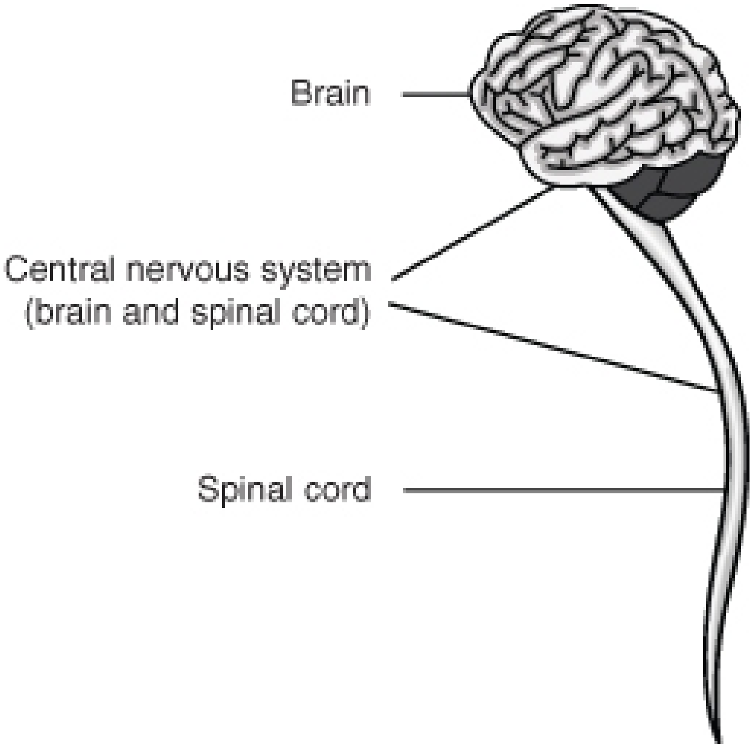

Figure 1.12: The components of the central nervous system (CNS).

The Brain

The brain is the most complex organ in the body. The brain contains about 100 billion neurons each of which can be connected to tens of thousands of other neurons within the brain. The brain is the source of what makes us human; the conscious mind. The mind is the set of cognitive processes related to perception, interpretation, imagination, memories, and language. Beyond cognitive functions, the brain regulates processes related to homeostasis such as respiration and heartbeat. An average adult human brain weighs between 1 and 1.5 kg (3 lb). An adult brain uses about 20-25% of the total energy used by the body, while the developing brain of an infant consumes around 60% of total energy used by the body.

The brain can be classified by the processes its different parts control. The **cerebrum** generally controls conscious functions such as problem-solving and speech, while the midbrain and the brain stem are more involved with unconscious (autonomic) functions such as breathing, heartbeat, and temperature regulation.

The cerebellum is involved in coordination and control of body movement. For a video of ”Brain Basics,” see http://www.teachers.tv/video/13838.

Cerebrum

The cerebrum is what most people would think of as the ”brain.” The cerebrum lies on top of the brainstem. It is made up of two cerebral hemispheres, which are shown in **Figure** 1.13. The two cerebral hemispheres are connected to each other at the corpus callosum, the light-colored X-shaped structure in the center of the image. The corpus callosum is a wide, flat bundle of axons found deep inside the brain. Mammals (including humans), have the largest and most well-developed cerebrum among all species.

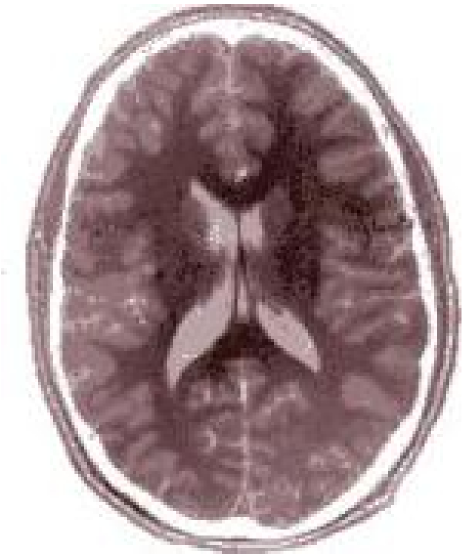

Figure 1.13: A magnetic resonance image (MRI) of the human brain in which the two hemispheres of the cerebrum can be seen.

Each hemisphere of the cerebrum can be divided into four parts, or lobes. These are: the frontal lobe, the parietal lobe, the temporal lobe, and occipital lobe. Researchers have identified a number of functional areas within each lobe, some of which are listed in **Table** 1.2. Both hemispheres look identical, but there are functional differences between them. For example, there are differences between the centers of function for spatial awareness between right and left-handed people. Each cerebral hemisphere receives sensory information and controls muscle movements of the opposite side of the body. The right hemisphere controls the left side of the body, and the left hemisphere controls the right side of the body.

Table 1.2: **Functions Controlled by the Cerebral Lobes**

Lobe	Functions
Frontal	Speech, intellectual function (reasoning, abstract thought), touch
Parietal	Speech, taste, reading
Temporal	Hearing, smell
Occipital	Vision

Brain Damage from Concussions: http://www.cnn.com/2009/HEALTH/01/26/athlete.brains/index.html

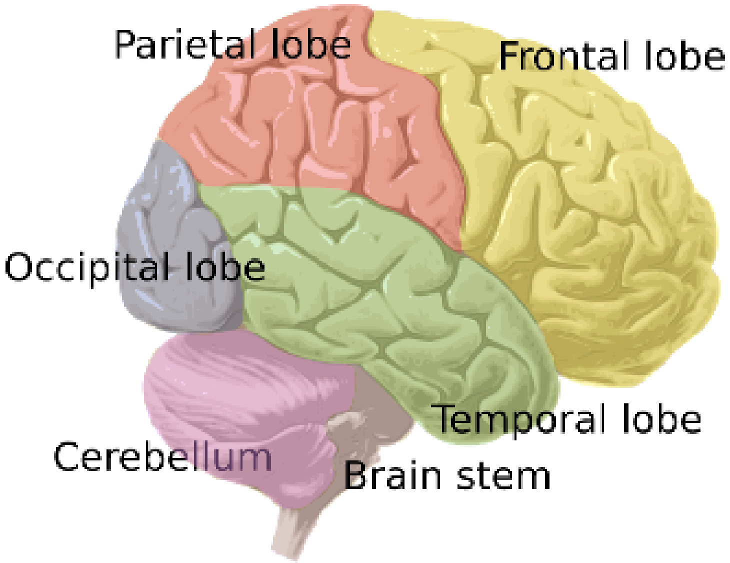

Figure 1.14: The lobes of the cerebral cortex-frontal, temporal, occipital, and parietal. The cerebellum (purple) and brain stem (gray) are not part of the hindbrain. In vertebrates, a gross division into three major parts is used.

The **cerebral cortex** is the highly-folded outer layer of the cerebrum that is between 2 mm and 4 mm thick. The lobes that make up the cerebral cortex, shown in **Figure** 1.14, are named after the skull bones that cover those areas of the brain. The many folds in the cortex allow for the large surface area of the brain to fit inside the skull. The cerebral cortex controls higher functions, such as consciousness, reasoning, emotions, and language. It also controls sensory functions such as touch, taste, smell, and responses to external stimuli. In the cerebrum, and found below the cerebral cortex, is the white matter. White matter is made up of myelinated axons that act as ‘‘cables” that link up certain parts of the right and left hemispheres.

Diencephalon

The **diencephalon** is the region of the brain that includes structures such as the thalamus, the hypothalamus, and a portion of the pituitary gland. The thalamus is believed to ‘‘translate” sensory signals for the cerebral cortex. The thalamus also plays an important role in regulating states of sleep and wakefulness. The hypothalamus gland controls certain metabolic processes and other autonomic activities such as body temperature, hunger, thirst, and circadian cycles. The hypothalamus also makes and releases neurotransmitters that control the action of the pituitary gland. The thalamus, hypothalamus, and hippocampus together are considered part of a set of structures called the limbic system. The limbic system is considered the ‘‘emotional center” of the brain.

Brain Stem

Sometimes called the ‘‘lower brain,” the **brain stem** is the lower part of the brain that is joined to the spinal cord. There are three parts to the brainstem: the midbrain, the pons, and the medulla oblongata, shown in Figure 15. The midbrain is more involved with unconscious, autonomic functions. The **midbrain** deals with several types of sensory information including sound and sight. It also “translates” sensory information to be sent to the forebrain. The brainstem also helps coordinate large body movements such as walking and running. The pons relays messages to different parts of the brain (the cerebrum and cerebellum), and helps regulate breathing. Some researchers propose that it has a role in dreaming. The medulla oblongata, also called the medulla, shares some of the function of the pons. It controls several homeostatic functions that you are usually unaware of, such as breathing, heart and blood vessel activity, swallowing, and digestion.

One of the brain stem’s most important roles is that of an “information highway.” That is, all of the information coming from the body to the brain (sensory) and the information from the cerebrum to the body (motor) go through the brain stem. Sensory pathways for such things as pain, temperature, touch, and pressure sensation go upward to the cerebrum, and motor pathways for movement and other body processes go downward to the spinal cord. Most of the axons in the motor pathway cross from one side of the CNS to the other as they pass through the medulla oblongata. As a result, the right side of the brain controls much of the movement in the left side of the body, and the left side of the brain controls much of the movement in the right side of the body.

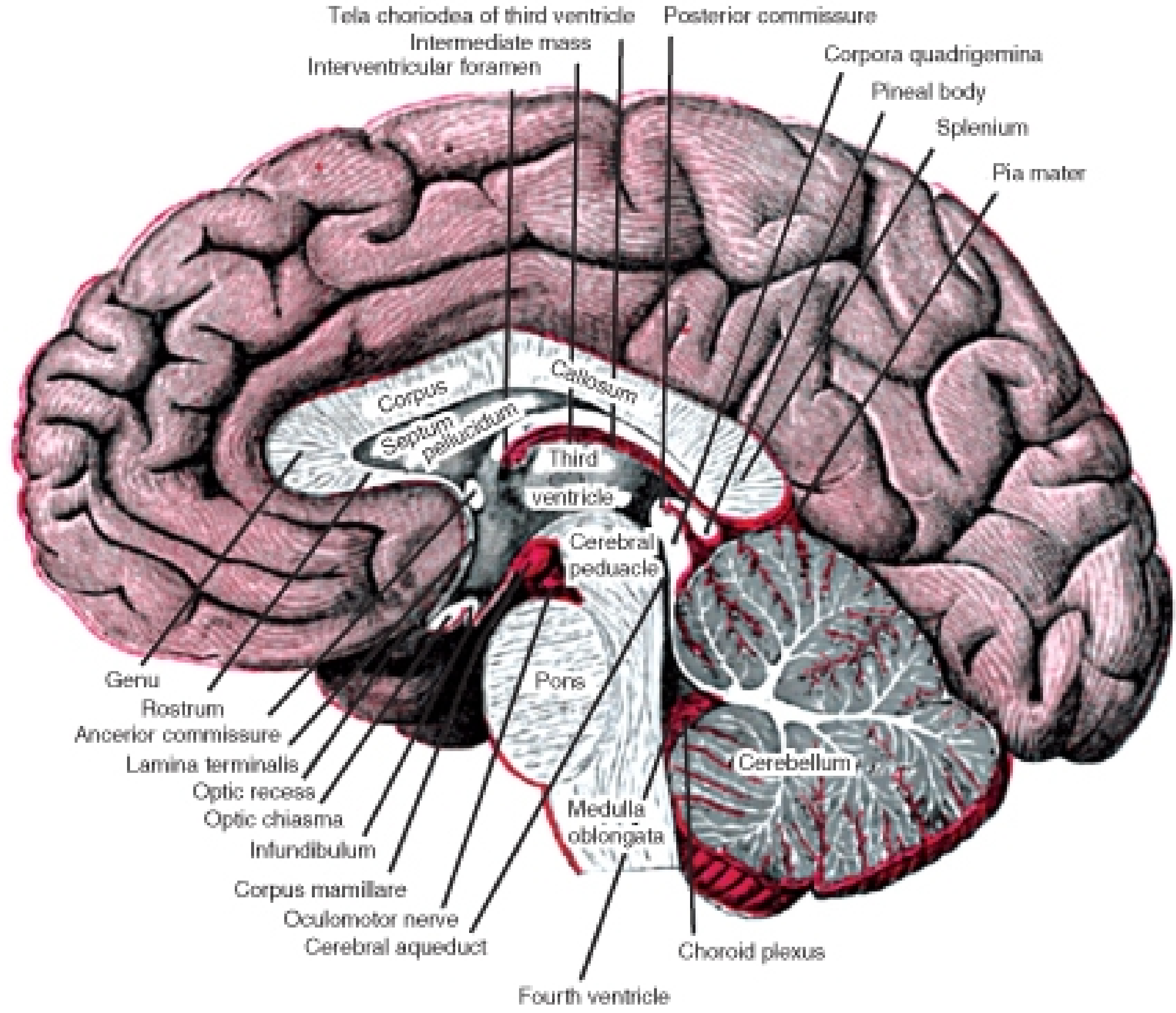

Figure 1.15: The locations of the brainstem and cerebellum. The brainstem is in the center of this image. It is made up of the pons, medulla oblongata, and the midbrain. The cerebellum is the red structure to the right of the brainstem.

Cerebellum

The **cerebellum** is found just below the occipital lobe of the cerebrum. It plays an important role in coordination and the control of body movements. Many nerve pathways link the cerebellum with motor neurons, which are neurons that send information to the muscles causing them to move, and a group of nerves that provides information on the position of the body in space. The cerebellum processes information from both these pathways, and uses the feedback on body position to fine-tune body movements. Hand-eye coordination is an example of such a function. If the cerebellum is damaged, there will not be paralysis, but the fine movement of the body (such as hand-eye coordination), balance, posture, and the ability to learn new motor skills will be negatively affected. The cerebellum is the purple structure in **Figure** 1.14. A section of the cerebellum is shown in **Figure** 1.15.

Spinal Cord

The **spinal cord** is a thin, tubular bundle of nervous tissue that extends from the medulla oblongata and continues to the lower back, where it ends in a group of fibrous extensions. It is protected by the spinal vertebrae. The main function of the spinal cord is as an information superhighway that links the sensory messages from the body to the brain. The outer cortex of the cord contains white matter (myelinated sensory and motor neurons). The central region, the grey matter, is made up of unmyelinated neurons. A cross section of the spinal cord is shown in **Figure** 1.16.

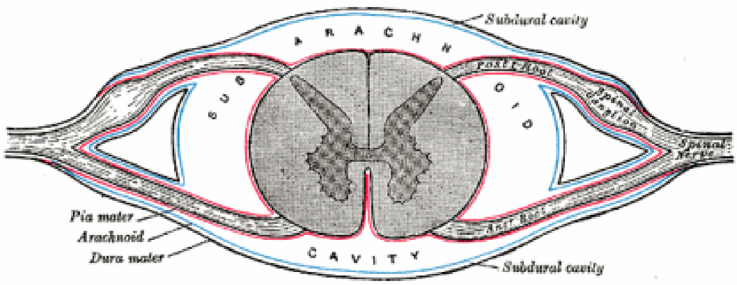

Figure 1.16: A cross section of the spinal cord. The central butterfly-shaped area is the gray matter and the area that surrounds it is the outer cortex (made up of white matter). Instructions go to the body

Peripheral Nervous System

The peripheral nervous system (PNS) consists of the nervous tissue that lies outside the central nervous system, shown in **Figure** 1.17. The nervous tissue of the peripheral nervous system serves the limbs and organs. The central nervous system interacts with the peripheral nervous system through twelve pairs of cranial nerves that connect the brain to areas of the head and neck and 31 pairs of spinal nerves that connect the spinal cord (and CNS) to the rest of the body, such as the internal organs, arms, and legs. A **nerve** is an enclosed, cable-like bundle of axons. Unlike the central nervous system, the peripheral nervous system is not protected by bone, making it more vulnerable to toxins and injuries.

Spinal nerves originate from the spinal cord. They control functions of the rest of the body. Each spinal nerve has a dorsal root and a ventral root, which are shown in **Figure** 1.18. The **dorsal root** is the "nerve highway" that carries sensory information from sensory receptors in the body to the CNS. The **ventral root** contains axons of motor neurons which carry information away from the CNS to the muscles and glands of the body.

These two nerve ‘‘highways” are actually parts of two subdivisions of the PNS. The **sensory division**, also known as the afferent division, carries sensory information from sensory receptors in the body to the CNS. The sensory division keeps the CNS constantly updated on events happening inside and outside the body. The **motor division**, or efferent division, carries nerve impulses from the CNS to the muscles, glands and organs of the body. The nerve impulses of the motor division cause muscles to contract and cause glands to secrete chemical signals.

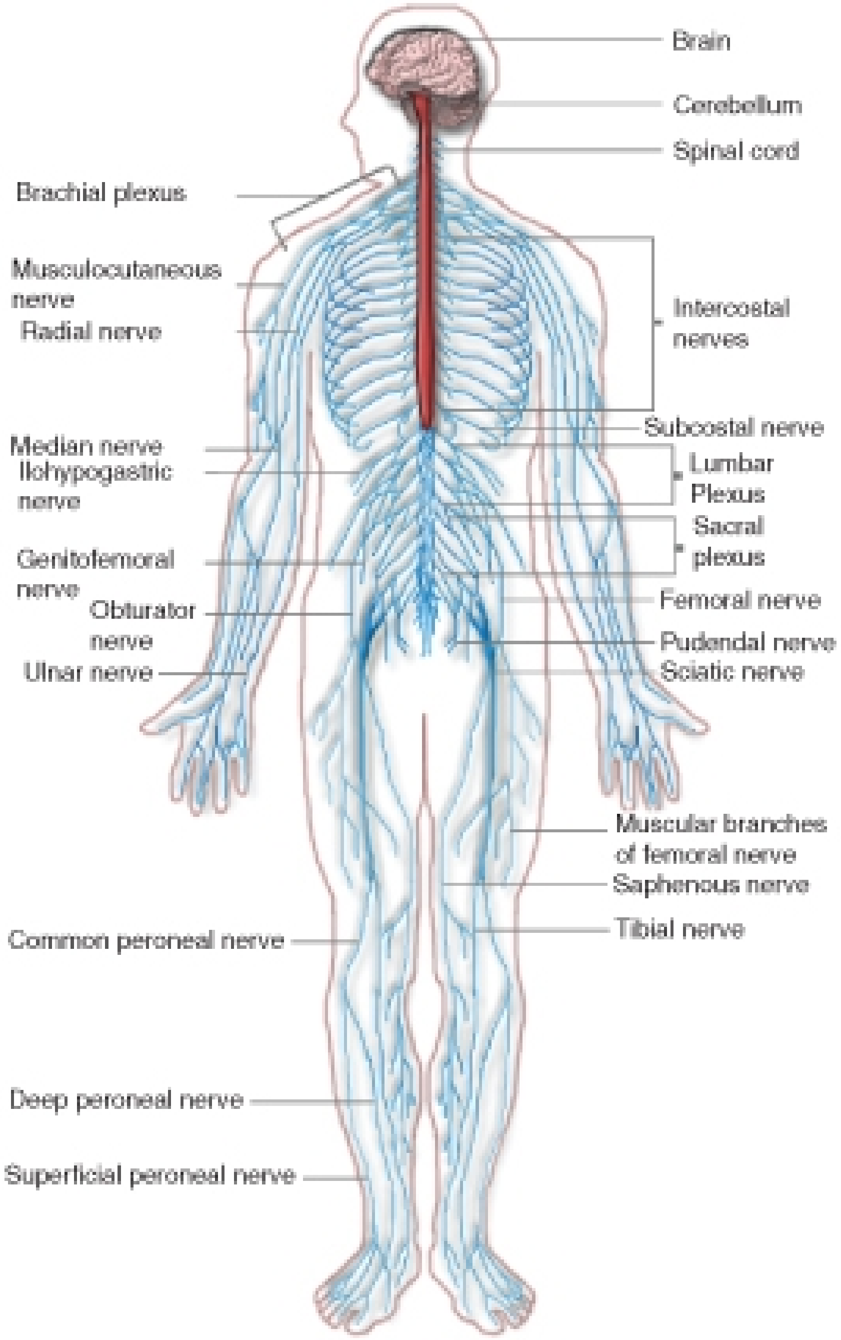

Figure 1.17: The peripheral nervous system (PNS). The peripheral nervous system extends from the CNS and reaches out to all parts of the body, from the cranial nerves found in the head to the plantar nerves in the tips of the toes.

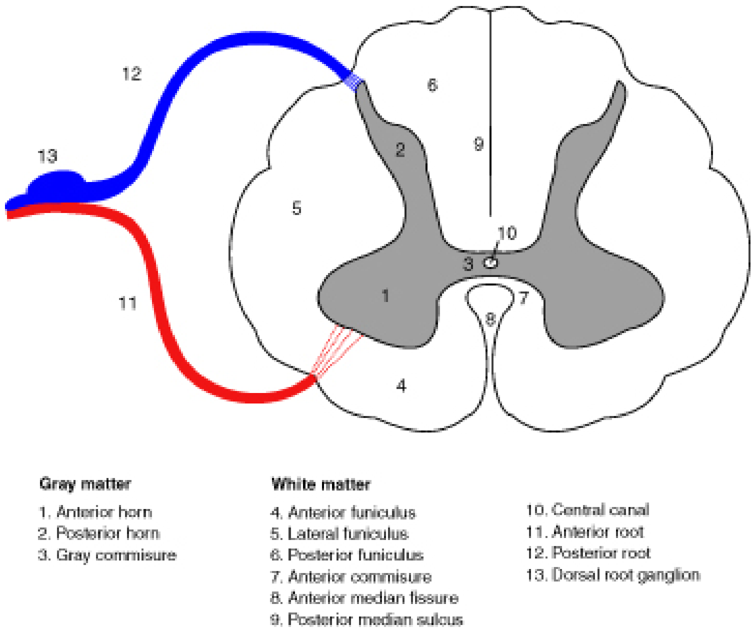

Figure 1.18: A cross section of the spinal cord. The central butterfly-shaped area (1, 2, 3) is the gray matter, the outer cortex is the white matter. Instructions going to the body

Somatic and Autonomic Nervous Systems

The motor division of the peripheral nervous system is divided into the somatic nervous system and the autonomic nervous system:

The **somatic nervous system** is the part of the PNS that is associated with the conscious (voluntary) control of the body through the movement of skeletal muscles and the perception of external stimuli through senses such as touch, hearing, and sight. The system includes all the neurons connected with muscles, skin and sense organs. The somatic nervous system is made up of sensory nerves that receive sensory information from the external environment, and motor nerves responsible for muscle contraction.

Together with interneurons, the sensory and motor neurons are found in a reflex arc. A **reflex** is an automatic (involuntary) action caused by a defined stimulus and carried out through a reflex arc. For example, a person stepping on a sharp object would start the reflex action through the creation of a stimulus, (pain) within specialized pain receptors located in the skin tissue of the foot. The resulting stimulus would be passed along sensory neurons to the spinal cord. This stimulus is usually processed by an interneuron to create an immediate response to pain by initiating a motor response in the muscles of the leg which pull the foot away from the object. This reflexive action would occur as the pain sensation is arriving in the brain. A reflex arc is shown in **Figure** 1.19.

The **autonomic nervous system** (**ANS**) is the part of the peripheral nervous system that maintains homeostasis in the body. Your body carries out most of these maintenance activities without your conscious control, which is why the autonomic nervous system is also called the involuntary nervous system. The ANS has far reaching effects, such as the control of heart rate, digestion, respiration rate, salivation, and perspiration. Some autonomic nervous system functions work in line with the conscious mind, such as breathing.

The ANS is also made up of the sensory and motor neurons that send messages to and from the internal organs. These neurons form reflex arcs that pass through the medulla oblongata. This explains why even a person's cerebrum may experience trauma, yet their cardiovascular, digestive and respiratory functions

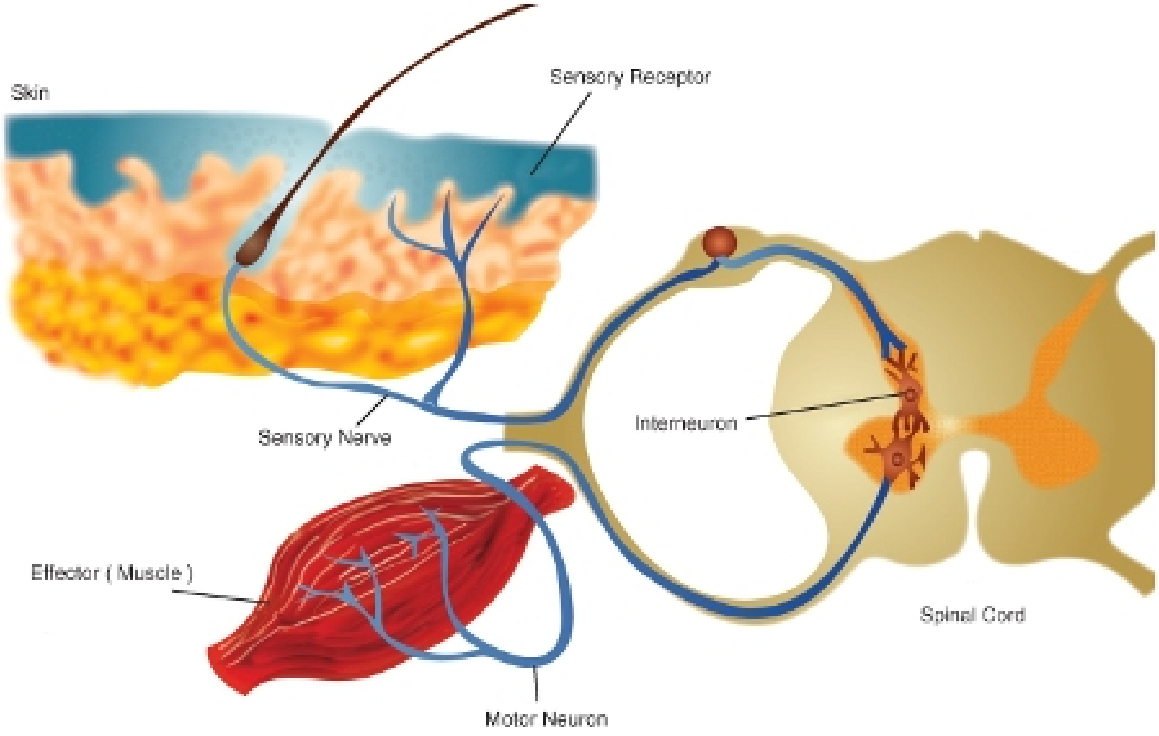

Figure 1.19: The components of a reflex. A sensory receptor that detects a stimulus and sends nerve signals to the spinal cord. These signals activate motor neurons that lead back to the effector (muscle).

will continue even if higher level functions such as awareness and consciousness, are lost. Such a low level of brain functioning is referred to as a vegetative state.

The ANS has two subdivisions: the sympathetic division and parasympathetic division. The **sympathetic division** generally stimulates body systems during emergency situations. It gets the body ready for "fight or flight," which would probably be required by the situation shown in **Figure** 1.20, while the **parasympathetic division** controls non-emergency functions such as digestion. The relationship between the divisions of the nervous system is illustrated in **Figure** 1.21.

Sense Organs and Sensory Perception (overview from HHMI http://www.hhmi.org/senses/)

Your senses are your body's means of making sense of the information your nervous system receives from inside your body and from the outside world. Your senses enable you to adapt to change in your environment and survive. The sensory division of the peripheral nervous system is organized into highly developed **sense organs**, which are groups of tissues that work together in responding to a specific kind of physical stimulus, such as the stimulus in **Figure** 1.22. The sense organs correspond to a defined region (or group of regions) within the brain where the nerve signals are received and interpreted. Your sense organs include your eyes, ears, nose, mouth, and skin. They all have sensory receptors that are specific for certain stimuli. For example, the nose has sensory receptors for odors (smells). Sensory neurons send nerve impulses from sensory receptors to the central nervous system. The brain then interprets the nerve impulses to form a response.

A sensory receptor is a cell, or a group of cells that detect stimuli. Sensory receptors can be classified based on the type of stimuli to which they respond.

Figure 1.20: Watch out! A situation in which your sympathetic nervous system (and hopefully your somatic nervous system), would be firing at full speed.

- **Chemoreceptors** respond to chemical stimuli.
- **Mechanoreceptors** respond to mechanical stress or strain (movement).
- **Thermoreceptors** respond to temperature changes.
- **Photoreceptors** respond to variations in light.
- **Baroreceptors** respond to pressure.

Specific areas of the brain interpret information from each sense organ. For example, regions of the occipital lobe interpret nerve impulses that come from the sensory receptors of the eyes, and regions of the temporal lobe interpret sensory information from the ears through the nerves that enter the brain in these areas, as shown in **Figure** 1.23. It is generally agreed that there are at least seven different senses in humans. These are sight, sound, taste, smell, touch, balance, and body awareness (the sense of knowing where the regions of your body are located at any one time). At least two other senses that humans do not have are observed in other organisms. Examples include electroreception, the ability to detect electric fields, and magnetoreception, the ability to detect magnetic fields.

Sight

Sight or vision describes the ability of the brain and eye to detect certain wavelengths of electromagnetic radiation (light), and interpret the image as ”sight.” Different receptors are responsible for the perception of color (the frequency of photons of light) and perception of brightness (number of photons of light). Photoreceptors are found in the retina, shown in **Figure** 1.24.

The structure of the eye owes itself completely to the task of focusing light onto the retina, the light-sensitive inner layer of the eye. First, light passes through a clear protective layer called the **cornea**, shown in **Figure** 1.24. Light then passes through the **pupil**, which is the opening in the iris, and into the interior of the eye. After passing through the pupil, the light then travels through the lens, a transparent, biconvex structure that, along with the cornea, helps to focus light on the retina. Muscles attached to the lens change the shape of the lens to bend the light rays so that they focus on the retina, as shown in **Figure** 1.25. Light hitting the retina causes chemical changes in the photosensitive cells of the retina, the products of which trigger nerve impulses which travel to the brain along the optic nerve.

The retina has two forms of photosensitive cells important to vision—rods and cones. **Rod cells** are

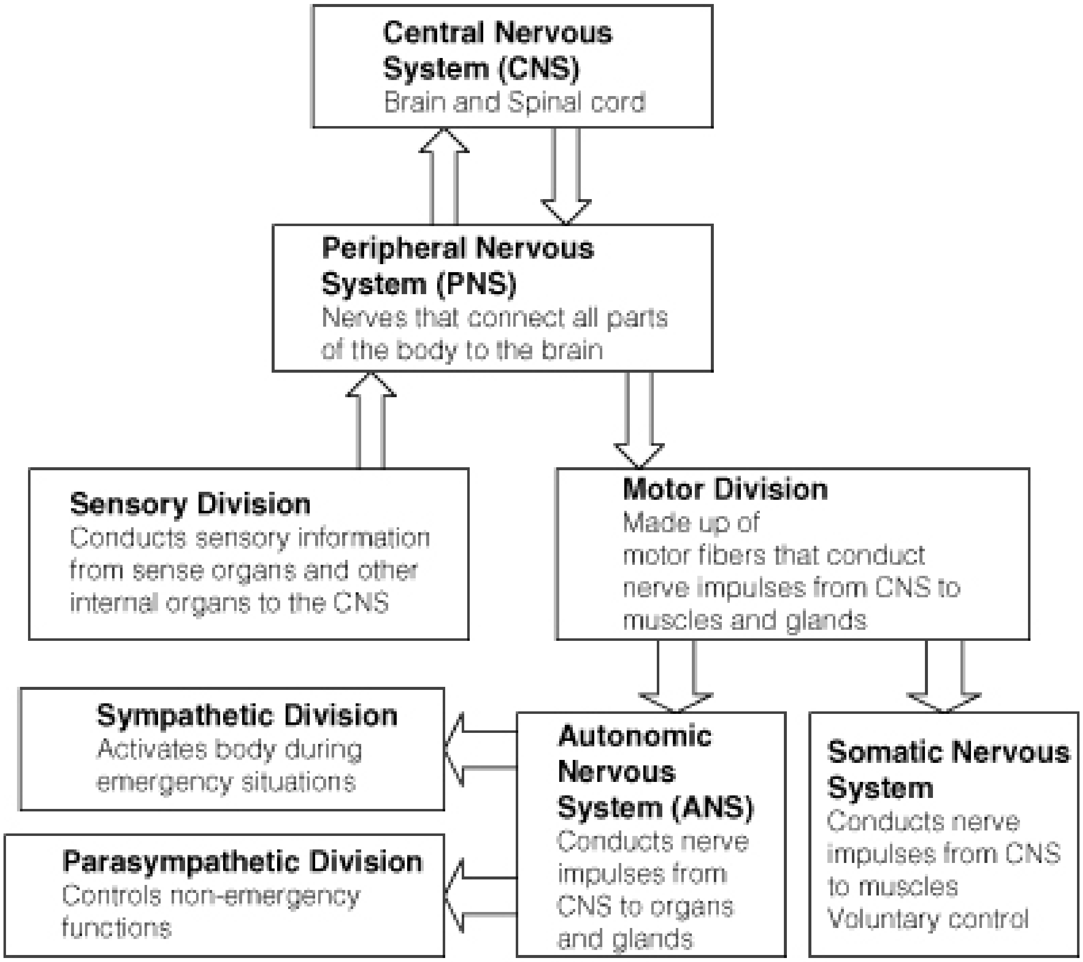
Central Nervous System (CNS)
Brain and Spinal cord
Peripheral Nervous System (PNS)
Nerves that connect all parts of the body to the brain
Sensory Division
Conducts sensory information from sense organs and other internal organs to the CNS
Motor Division
Made up of motor fibers that conduct nerve impulses from CNS to muscles and glands
Sympathetic Division
Activates body during emergency situations
Parasympathetic Division
Controls non-emergency functions
Autonomic Nervous System (ANS)
Conducts nerve impulses from CNS to organs and glands
Somatic Nervous System
Conducts nerve impulses from CNS to muscles
Voluntary control

Figure 1.21: Levels of Organization of the Nervous System.

Figure 1.22: Can you smell these fresh, juicy oranges and kumquats? Your senses of smell, taste and sight are also important in developing an appetite. Just think of how appetizing these fruits would be if they were blue, crunchy, and smelled like burned toast.

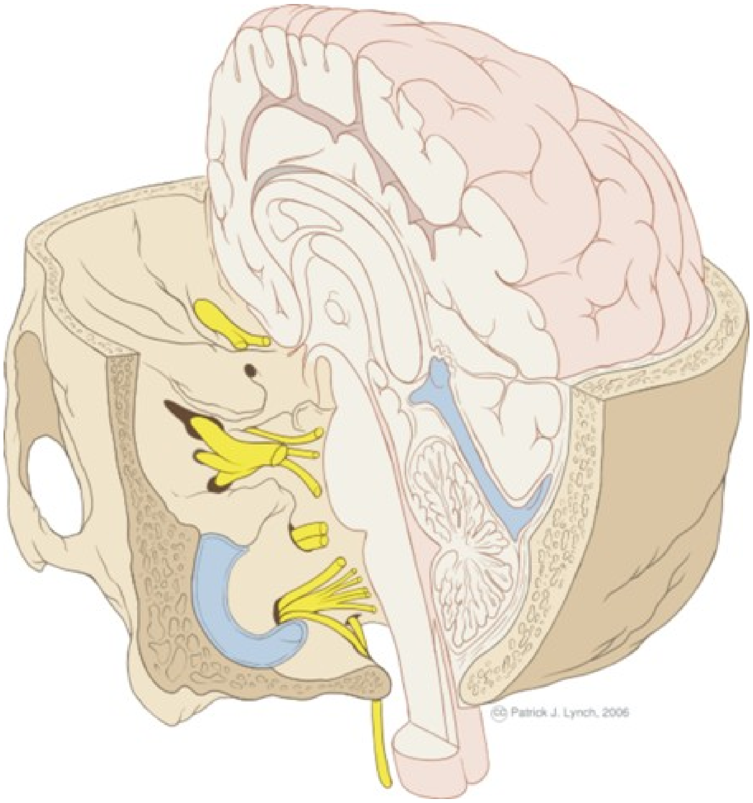

Figure 1.23: The entry of sensory nerves into the brain. Among other nerves, the sensory nerves for smell, sight, hearing, and taste (yellow structures) can be seen entering the skull. You can also see how the cerebrum, thalamus, cerebellum, and brain stem are nested within the skull.

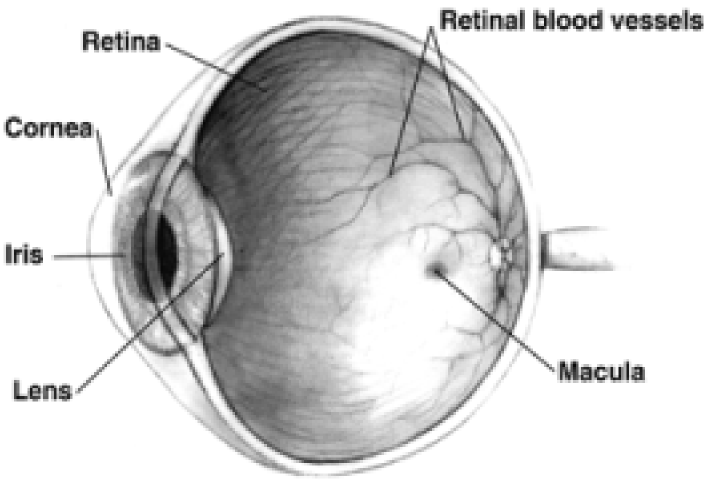

Figure 1.24: The structure of the eye. The macula is a spot near the center of the retina that has a diameter of about 1.5 mm. Near its center is the fovea, a small pit that contains the largest concentration of cone cells in the eye and is responsible for central vision. The macula is the point of sharpest vision. A video of the human eye is available at

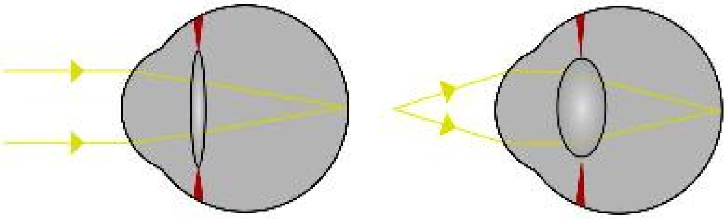

Figure 1.25: Focusing light in the retina. This diagram shows how light from a distant source is bent by the stretched lens to strike the retina, and how light from a closer source is bent even more sharply by the relaxed lens to strike the retina.

highly sensitive to light which allows them to respond in dim light and dark conditions, but, they cannot detect color. These are the cells which allow humans and other animals to see by moonlight, or in a dimly-lit room. This is why the darker conditions become, the less color objects seem to have. **Cone cells** respond to different wavelengths of bright light to initiate a nerve impulse. They are also responsible for the sharpness of images. Cones do not respond well in poor light conditions, which is the reason why you see things in dim light as fuzzy shades of gray.

Humans have three different types of cone cells that respond to different wavelengths of light. These cone cells contain a pigment that absorbs the energy from different wavelengths of light to initiate a nerve impulse. Activation of the visual pigments by certain wavelengths of light opens ion channels on the membrane of the cone or rod cell. This leads to an action potential that is carried by the millions of neuron axons that make up the optic nerve to the visual centers of the brain. The brain integrates the nerve impulses from the cone cells and perceives the world in all the colors of the visual spectrum. A person who is colorblind has damaged or missing cones, and is unable to perceive certain colors.

Hearing

Hearing is the sense of sound perception that results from the movement of tiny hair fibers in the inner ear. These hairs detect the motion of a membrane which vibrates in response to changes in air pressure. Sound can also be detected as vibrations that are conducted through the body. Sound wave frequencies that are too low or too high to be heard by the ear can be detected this way. Audible sound is sensed by the ear.

Animations of hearing: http://www.hhmi.org/biointeractive/neuroscience/cochlea.html

The folds of cartilage surrounding the outer ear canal are called the **pinna**. Sound waves are gathered by the pinna, and channeled down the **auditory canal**, a tube-shaped opening of the ear which ends at the tympanic membrane, or **eardrum**.

Sound waves traveling through the ear canal hit the eardrum and cause it to vibrate. This wave information travels across the air-filled middle ear cavity through a group of three tiny, delicate bones: the **hammer**, the **anvil**, and the **stirrup**, shown in **Figure** 1.26. This group of bones transfers the eardrum vibrations to another membrane called the oval window. The oval window separates the middle ear from the inner ear. The inner ear contains the cochlea.

The **cochlea** is a coiled tube that is filled with a watery liquid, which moves in response to the vibrations coming from the middle ear through the oval window. As the fluid moves, thousands of mechanoreceptors called **hair cells** bend, releasing a neurotransmitter. The neurotransmitter causes an action potential in the neurons of the auditory nerve. The action potential travels along the auditory nerve to structures in the brainstem, then to the thalamus, and then to the auditory centers of the brain in the temporal lobe of the cerebral cortex.

A very strong movement of the fluid within the cochlea, caused by very loud noise, can kill hair cells. This is a common cause of partial hearing loss and is the reason why users of firearms or heavy machinery should wear earmuffs or earplugs. Destruction of the hair cells usually leads to permanent hearing loss because once destroyed, the hairs do not generally grow back.

Balance and the Ears

It might be hard to believe, but your ears are also in charge of your sense of balance! The **semicircular canals** are three fluid-filled interconnected tubes found inside each ear. They can be seen in **Figure** 1.26, directly above the cochlea. The canals are positioned at angles between 95 to 115 degrees relative to one another. The angles between the canals are not perpendicular, so movements of the head cause movement

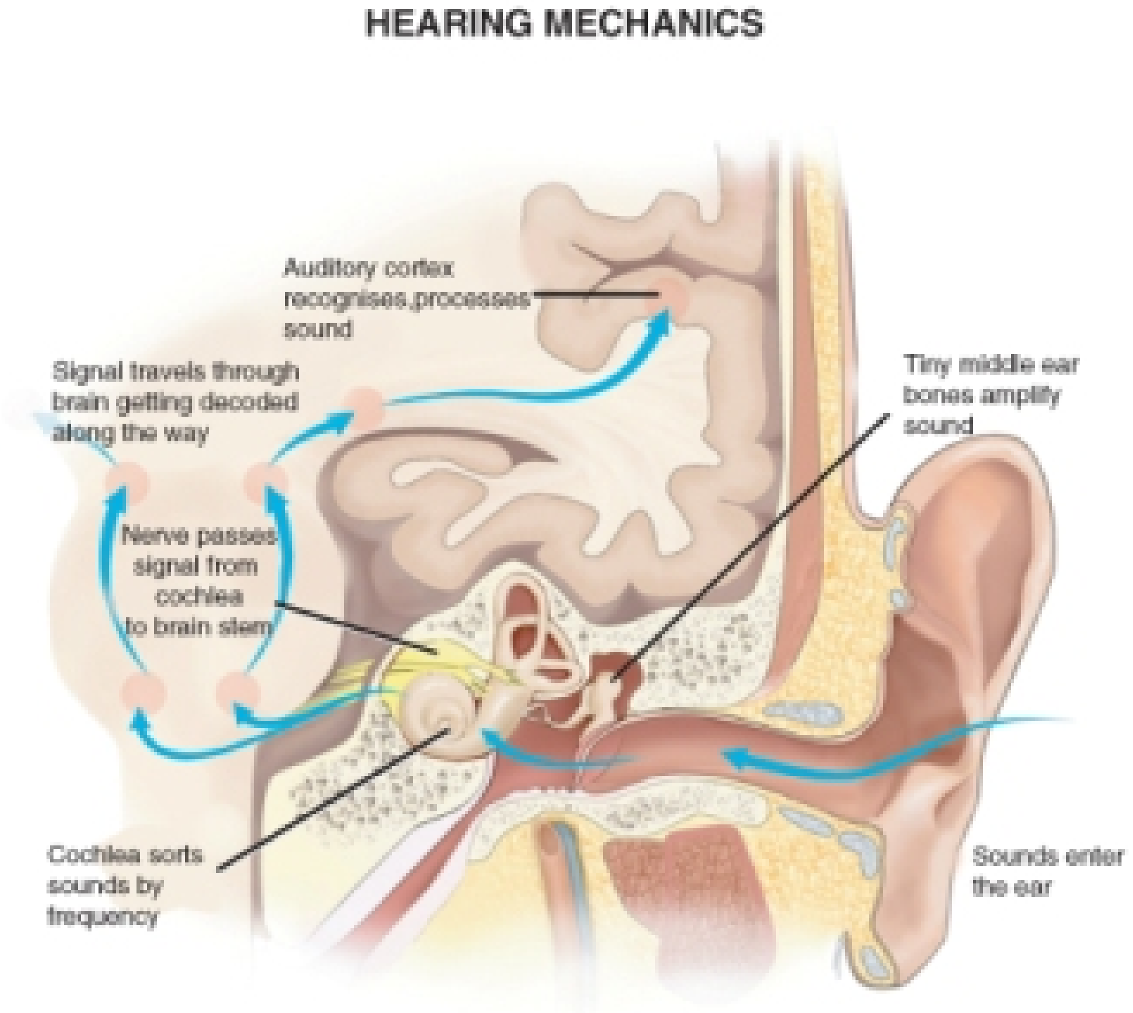
HEARING MECHANICS
Auditory cortex recognises,processes sound
Signal travels through brain getting decoded along the way
Tiny middle ear bones amplify sound
Nerve passes signal from cochlea to brain stem
Cochlea sorts sounds by frequency
Sounds enter the ear

Figure 1.26: The detection of sound by your ear.

of fluid in two canals at the same time.

Each canal is filled with fluid called endolymph and motion sensors with little hairs, called cilia, line each canal. Movement of the head and body cause the endolymph in the canals to move about. The hair cells sense the strength and direction of the fluid's movement and send electrical signals to the cerebellum which interprets the information and responds to help keep the body's sense of balance. The interaction of the semicircular canals and the cerebellum allow the performer in **Figure** 1.27 to do his act.

Figure 1.27: Good balance required! This performer

When the sense of balance is interrupted it causes dizziness and nausea. Balance can be upset by an inner ear infection, a bad head cold or a sinus infection, or a number of other medical conditions. It can also be temporarily disturbed by rapid and repetitive movement, for example riding on a merry-go-round or spinning around in a circle.

Taste and Smell

Taste is one of the two main chemical senses, the other being smell. There are at least four types of taste receptors on the tongue. Taste stimuli from each receptor type send information to a different region of the brain. The four well-known receptors detect sweet, salt, sour, and bitter. The existence of a fifth receptor, for a sensation called umami, was confirmed in 2000. The umami receptor detects the amino acid glutamate, which causes a savory, ‘‘meaty” flavor in foods.

The chemoreceptors of the mouth are the taste cells that are found in bundles called taste buds. Most of the taste buds are embedded within the tiny papillae or ‘‘bumps” that cover the tongue, shown in **Figure** 1.28. Each receptor has a different way of detecting certain compounds and starting an action potential

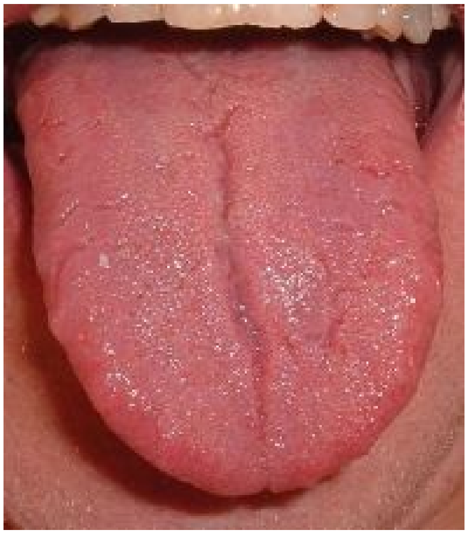

Figure 1.28: The location of taste buds. Most of the taste buds in the mouth are embedded in the papillae, the little bumps that cover the tongue. The deep groove (fissure) that runs down the center of the tongue in this photo is a common and perfectly normal condition.

which alerts the brain. The compounds bind to receptors in the taste cells and stimulate neurons in the taste buds. The action potential moves along the facial nerves to the thalamus and then to the taste center of cerebral cortex for interpretation by the brain. The tongue can also feel sensations that are not generally called tastes. These include: temperature (hot or cold), coolness (as in ‘‘minty” or ‘‘fresh”), spiciness or hotness (peppery), and fattiness (greasy).

Smell is the other ”chemical” sense. The chemoreceptors of smell are called **olfactory receptors.** About 40 million olfactory receptor neurons line the nasal passages. Different odor molecules bind to and excite specific olfactory receptors. The combination of excitatory signals from different receptors makes up what we identify as ‘‘smell.” Signals from the olfactory receptors travel along nerves to the olfactory bulb in the brain where they then move to the smell center in the frontal lobe of the cerebral cortex. Olfactory receptor neurons in the nose differ from most other neurons in that they die and regenerate on a regular basis. A dog’s keen sense of smell is due to the large area of its nasal passages that are covered by olfactory receptors, and the large number of nerves that bring nerve impulses from the receptors to its brain. For example, the area in which olfactory receptors are located inside the human nose (called the olfactory epithelium), which is shown in **Figure** 1.29, measures about 12 cm^2. The olfactory epithelium of some dogs’ noses can measure about 150 cm^2!

Have you ever noticed that you cannot taste anything when your nose is stuffed up? That is because your senses of smell and taste are closely linked. This is due to the fact that your nasal cavity, located behind the nostrils, connects to your mouth at the back of your throat, as shown in **Figure** 1.29. Your olfactory receptors and taste receptors both contribute to the flavor of food. Your tongue can only tell among a few different types of taste, while your nose can distinguish among hundreds of smells, even if only in tiny amounts.

Touch, Pressure, and Pain

Touch is the sense of pressure perception, which is generally felt in the skin. There are a variety of pressure receptors that respond to variations in pressure and tension. Mechanoreceptors are most numerous on the tongue, lips, face, palms (including fingertips), and soles of the feet.

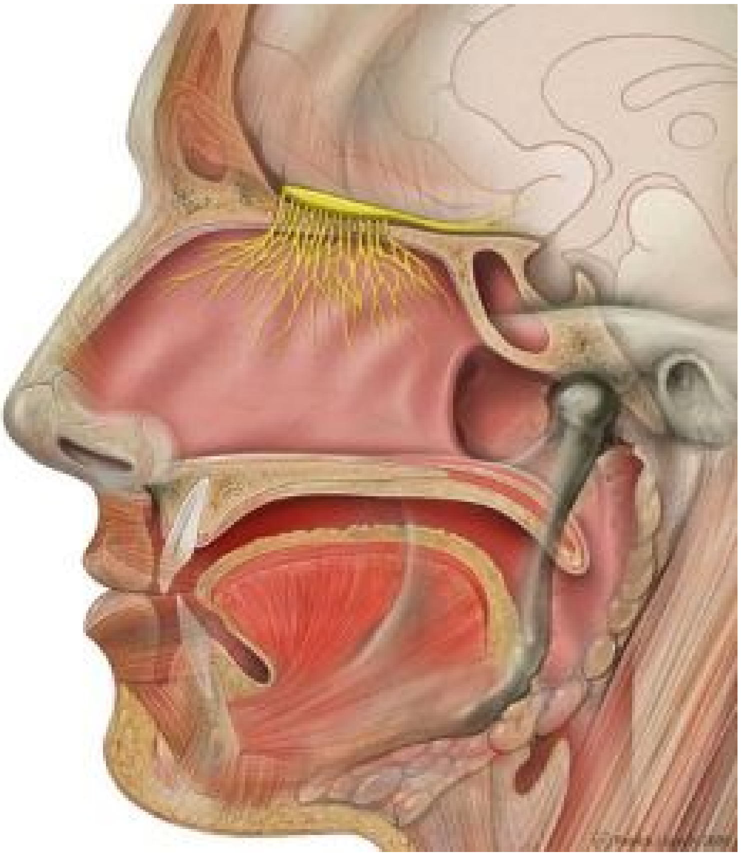

Figure 1.29: The location of olfactory nerves. Olfactory receptors and their associated nerves (yellow) line the top of the nasal passages. Nerve messages from the receptors are sent to the brain to be interpreted as certain smells.

There are several types of pain receptors, called **nociceptors**, which respond to potentially damaging stimuli. They are mostly found in the external parts of the body such as the skin, cornea, and mucous membranes, but are also found in muscles, joints, and some internal organs. Nociceptors are classified according to the stimuli to which they respond: thermal, mechanical or chemical. But some receptors respond to many different damaging stimuli of a chemical, thermal, or mechanical nature. Thermal receptors are activated by potentially harmful heat or cold, temperatures above 45°C and below 5°C. Mechanical receptors respond to excess pressure, squeezing, or bending, the type of painful stimuli that a cactus such as the one in **Figure** 1.30 would cause. Together these nociceptors allow the organism to feel pain in response to damaging pressure, excessive heat, excessive cold and a range of chemicals, the majority of which are damaging to the tissue surrounding the nociceptor.

Figure 1.30: Mechanical pain receptors in your skin would warn you if you got too close to this prickly cactus.

Drugs and the Nervous System

A **drug** is any chemical or biological substance that affects the body's structure or functions. Drugs in the form of medicines are used to treat many illnesses and disorders. A **medicine** (or medication), is a drug that is taken to cure or reduce the symptoms of an illness. However, drugs, whether they are medicines, legal or illegal drugs, can be abused for the effects they have on the central nervous system (CNS). In fact many medical uses of drugs depend on the powerful effect they have on brain function. For example, anti-depression medicines are used to treat depression and anxiety disorders, and antipsychotic medicines are used to treat schizophrenia and bipolar disorder.

A **psychoactive drug** is a substance that affects the central nervous system by altering cognitive function. Change in cognitive function results in changes in how a person feels, thinks, perceives, and acts. Almost everyone has used a psychoactive drug at some time in their life, and many people take such drugs daily. For example, the coffee or tea that you may have drank to waken yourself up this morning, or the cola, energy drink, or chocolate that you had as a snack contain the psychoactive drug caffeine. Caffeine is a CNS stimulant that makes you feel less drowsy and more alert. Coffee beans, the most common source of caffeine, are shown in **Figure** 1.31.

Figure 1.31: Roasted coffee beans. Coffee beans are a common source of the stimulant caffeine. Other plant sources include the leaves of tea, cocoa, yerba mate, and guarana plants. These plants use caffeine as a means of protection against being eaten. The caffeine in the leaves of these plants can paralyze and kill the insects that feed upon them.

Drugs and the Brain: How Psychoactive Drugs Work

How we perceive stimuli, feel, think, and do is a result of neurons sending action potentials and neurotransmitters to each other and to other cells in the body. Psychoactive drugs affect how neurons communicate with each other. These drug molecules can alter neurotransmission, by blocking receptor proteins, mimicking neurotransmitters, or changing the amount of neurotransmitter in the synapse, shown in **Figure** 1.32, by blocking reuptake. In this way a psychoactive drug can change how we feel, think, and interact with the world. Sometimes such effects are beneficial, such as taking a prescribed painkiller (hydrocodone, for example), to ease the pain of a broken bone. Sometimes the effects are harmful, which could happen if the person continued to take the powerful painkiller long after their broken bone had healed. Some examples of psychoactive medicines are listed in **Table** 1.3.

Table 1.3: **Some Psychoactive Medicines and Their Uses**

Type	Uses	Example	Action
Anesthetics	Block pain and other sensations. Often induce unconsciousness, which allows patients to undergo medical procedures.	Lidocaine, nitrous oxide	Mimic the inhibitory neurotransmitter GABA, or increase the amount of GABA in the synapse which prevents an action potential.
Painkillers (analgesics)	Reduce the sensation of pain. Includes narcotics and non-steroidal anti-inflammatory drugs (NSAIDS)	Narcotics: morphine and codeine NSAIDS: aspirin and acetaminophen (paracetamol).	Drug molecules mimic endogenous opioids “natural painkillers,” such as endorphins, by binding to opioid receptors.

Table 1.3: (continued)

Type	Uses	Example	Action
Antidepressants	Antidepressants are used to treat disorders such as clinical depression, anxiety, and eating disorders	Selective Serotonin Reuptake Inhibitors (SSRIs); Monoamine oxidase inhibitors (MAOIs)	SSRIs: Block the uptake of the neurotransmitter serotonin by presynaptic neuron MAOIs: Prevent an enzyme from breaking down serotonin in the synapse. Both actions result in an increase of serotonin in the synapse.
Stimulants	Used to treat disorders such as attention deficit disorder and to suppress the appetite	Amphetamine salts	Increases extracellular levels of dopamine, norepinephrine and serotonin by various means
Antipsychotics	Used to treat psychoses such as schizophrenia and mania.	Chlorpromazine	Blocks dopamine receptors in post synaptic neurons
Cough medicines (antitussives)	Used to treat persistent coughing.	Dextromethorphan (DXM) and codeine	Inhibit the action of, the NMDA receptor in the post synaptic cell. Reduces action potential, similar in action to anesthetics

Drug Abuse

Psychoactive drugs bring about changes in mood and feelings that a user may find desirable, therefore many psychoactive substances are abused. **Drug abuse** is the repeated use of a drug without advice or guidance of a medical professional, and use for reasons other than for what the drug was originally intended. With continued use of a drug, a person might find that they cannot function normally without the drug, a state called **physical dependence**. However, note that physical dependence is not in itself bad, for example, a person who has diabetes is physically dependent on insulin injections. Their body cannot work properly without it. Emotionally or mentally needing a drug to be able to function normally is called **psychological dependence**. When a person continues to take a psychoactive drug, they eventually need to take larger doses of the drug to get the desired effect; this process is known as building a **tolerance** to the drug. Drug tolerance can involve both psychological and physical factors.

A person who is abusing a drug may eventually lose control of their drug-taking behavior, partly due to the changes the drug has caused in their brain, and partly due to learned drug-abuse behaviors (such as stealing and lying to get money or drugs). In the state of **addiction**, a drug addict's life and activities revolve around getting more of the drug to feed their habit, even if it leads to severe consequences such as getting arrested, dropping out of school, or isolation from friends and family. In a person who is addicted to a drug, the pattern of increasing dose due to tolerance can lead to a **drug overdose**, also known as

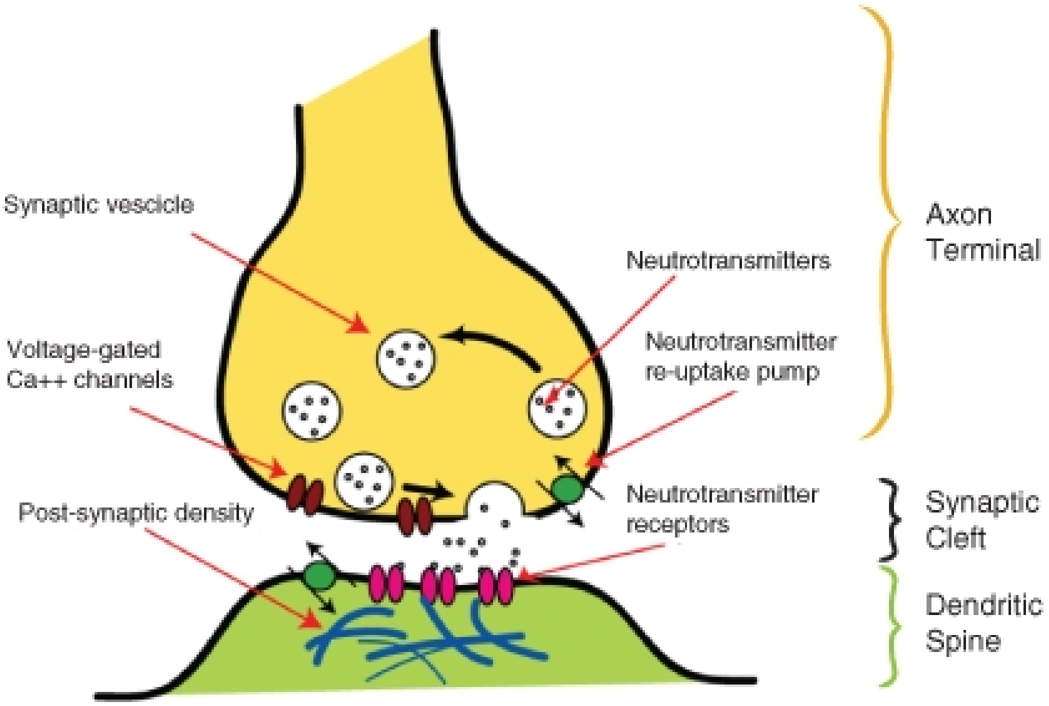

Figure 1.32: The release of neurotransmitter into the synaptic cleft. Depending on its method of action, a psychoactive substance may block the receptors on the post-synaptic neuron, or block reuptake or affect neurotransmitter synthesis in the pre-synaptic neuron.

an OD. A drug overdose is generally considered harmful and may lead to death. Drug dependence and addiction are caused by changes in the way neurons in the CNS send and receive neurotransmitters. It is for this reason dependency and addiction are treated as brain disorders by medical professionals.

Several classes of psychoactive drugs are commonly abused. **Stimulants** such as cocaine, nicotine, and amphetamine increase the activity of the sympathetic nervous system, the central nervous system, or both. Stimulants generally increase heart rate, blood pressure, and increase the sense of alertness. Some stimulants, such as caffeine, are used medicinally to increase or maintain alertness, and to counteract fatigue. High doses of stimulants can be fatal. A common source of nicotine is cigarette tobacco, shown in **Figure** 1.33.

Hypnotics, also known as **depressants**, such as alcohol, codeine, barbiturates, and benzodiazepines generally decrease the activity of the central nervous system. Depressants slow down brain function and give a drowsy or calm feeling. However, taking too much of a depressant drug can cause dangerously slow breathing and heart rates, and may result in death. Many depressants acting on the CNS do so by increasing the activity of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA), although there are many receptors that are affected by different depressants. GABA calms the activity of the CNS and promotes sleep. Drugs that stimulate the activity of this amino acid slow down brain function and cause a drowsy or calm feeling, so depressants are generally prescribed to relieve symptoms of anxiety or insomnia.

Hallucinogens, also known as psychedelic drugs, such as lysergic acid diethylamide (LSD), phencyclidine (PCP), and ketamine, are psychoactive drugs that do not increase or decrease a certain feeling or emotion, but rather they induce experiences, such as sensory distortions and “out-of-body experiences,” that are very different from those of ordinary consciousness. These experiences are often called trance-like states. The use of psychedelic drugs has been linked to a potential for brain damage.

Figure 1.33: Cigarettes are a common source of nicotine. Nicotine is a compound that is found in the leaves of the tobacco plant. It is a potent neurotoxin for insects, and was once used as an insecticide. In addition to the addictive nature of nicotine, long-term tobacco use carries significant risks of developing various cancers as well as strokes and severe cardiovascular and respiratory diseases.

There are many ways in which psychoactive drugs can affect the CNS. Each drug has a specific action on one or more neurotransmitters or receptors. Drugs that increase activity in particular neurotransmitter systems are called **agonists**. They act by increasing the synthesis of one or more neurotransmitters or reducing its reuptake from the synapses. Drugs that reduce neurotransmitter activity are called **antagonists**, and work by interfering with synthesis or blocking postsynaptic receptors so that neurotransmitters cannot bind to them. The drug ketamine, which is used as an anesthetic and a painkiller, blocks the action of the neurotransmitter glutamate. Diacetylmorphine (heroin) enhances the action of endorphins in the brain. Different drugs also affect different parts of the brain. For example, drugs that affect breathing, such as cough suppressants, affect the brainstem to stop the coughing reflex. Painkillers (analgesics) block pain messages coming through the spinal cord from the body. In **Figure** 1.34 the brainstem region is blue, and the spinal cord is yellow.

How Addiction Happens

The **neurobiological theory of addiction** proposes that certain chemical pathways are greatly changed in the brain of an addicted person. Almost all drugs that are abused affect a certain set of brain structures in the limbic system called the "brain reward system," shown in **Figure** 1.27. The neurotransmitter dopamine is commonly associated with the brain reward system. The system providing feelings of pleasure (the "reward"), that motivates a person to perform certain activities over and over again. Dopamine is released at synapses by neurons when a person has a pleasurable experience such as eating a favorite food, or eating when very hungry. Such mechanisms have evolved to ensure the survival of organisms.

Some drugs, such as cocaine, nicotine, amphetamines, and alcohol directly or indirectly increase the amount of dopamine in the limbic structures. The pleasurable feelings that these drugs produce trick the body into thinking that the drug is good,important for survival, and needs to be taken repeatedly. Drugs that directly affect the brain reward system are highly addictive. The stimulant nicotine, which is found in

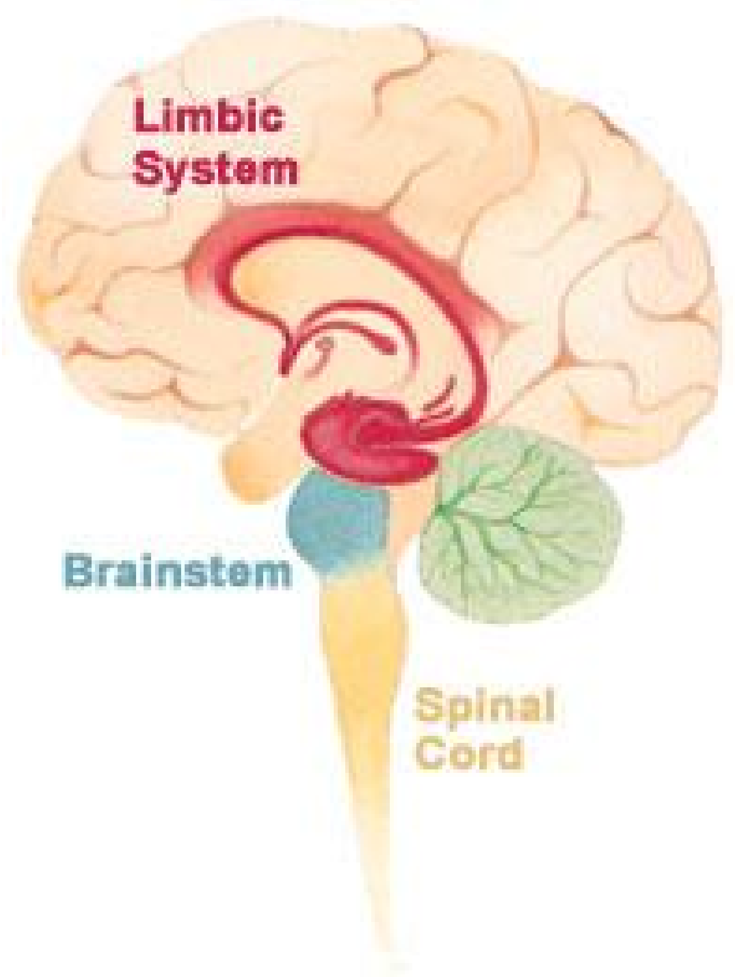

Figure 1.34: The limbic system (in red) includes structures in the human brain that have been linked to emotion, motivation, and emotional association with memory. The action of neurotransmitters in the limbic system is altered by addictive drugs.

tobacco, is highly addictive.

Cocaine is an example of a psychoactive drug that is both used as a medicine, and abused as a drug. Cocaine is highly addictive. It is a dopamine transporter blocker—it blocks the reuptake of dopamine by the presynaptic neuron. This action increases the amount of dopamine left in the synaptic cleft, so dopamine has a stronger effect on the postsynaptic neuron. Continued cocaine use causes a reduction in the number of dopamine receptors on the postsynaptic neuron. Eventually, the post synaptic neuron becomes understimulated because there are fewer dopamine receptors on it to respond to dopamine. At this point, more cocaine must be taken to stimulate the postsynaptic neuron into an action potential. If a person becomes dependent on the drug, they need cocaine for their body to act normally. If a person were to stop taking the drug at this point, their body would not be able to act normally, and they would experience a range of uncomfortable and painful symptoms called **withdrawal**. Symptoms of withdrawal include vomiting, diarrhea, and depression.

Many psychoactive substances are used or abused for their mood and perception altering effects, including those with accepted uses in medicine and psychiatry. Classes of drugs that are frequently abused include some of the drugs listed in **Table** 1.4. Drugs that are deemed by to have no medical uses and a high potential for abuse are usually illegal.

Not all drugs are physically addictive, but any activity that stimulates the brain reward system can lead to psychological addiction. Drugs that are most likely to cause addiction are drugs that directly stimulate the dopaminergic system, like cocaine, nicotine, and amphetamines. Drugs that only indirectly stimulate the dopaminergic system, such as psychedelics, are not as likely to be addictive.

Table 1.4: **Some Common Drugs of Abuse**

Psychoactive Drugs	Effects	Examples	Some Common Forms or Names
Stimulants	Elevate the central nervous system and raise level of alertness and wakefulness	Caffeine, cocaine, amphetamine, methamphetamine	Coffee, coke, meth, ecstasy (X)
Hallucinogens	Induce perceptual and cognitive distortions	LSD, psilocybin, mescaline, PCP	Acid, magic mushrooms, peyote, angel dust
Hypnotics	Depress the CNS, and induce sleep	Barbiturates, opioids (e.g. codeine, morphine, oxycodone), benzodiazepines, ethanol	Diazapam, alcohol
Analgesics	Induce euphoria, reduce sensation of pain	Codeine, morphine, ketamine, heroin, phencyclidine (PCP), tetrahydrocannabinol (THC)	Horse, angel dust, cannabis, marijuana

Lesson Summary

- Neurons are typically made up of a cell body, dendrites, and an axon. The cell body contains the nucleus and other organelles similar to other body cells. The dendrites extend from the cell body and receive a nerve impulse from another cell. The cell body collects information from the dendrites and passes it along to the axon. The axon is a long, membrane-bound extension of the cell body that passes the nerve impulse onto the next cell.

- Voltage is electrical potential energy that is caused by a separation of opposite charges across the membrane. The voltage across a membrane is called membrane potential. Membrane potential is the basis for the conduction of nerve impulses along the cell membrane. In an action potential, the cell membrane potential changes quickly from negative to positive as sodium ions flow into and potassium ions flow out of the cell through ion channels.
- A neurotransmitter is a chemical message that is used to relay electrical signals between a neuron and another cell. Neurotransmitter molecules are made inside the presynaptic neuron and stored in vesicles at the axon terminal.
- The central nervous system represents the largest part of the nervous system, and includes the brain and the spinal cord. The brain is the central control of the nervous system, and the spinal cord carries nerve impulses between the brain and the body, and from the body to the brain.
- The sense organs include the eyes, ears, nose, mouth, and skin. They all have sensory receptors that are specific for certain stimuli. The eyes have photoreceptors for sight. The ears have mechanoreceptors that interpret stimuli as sound and also endolymph that aids in body balance. The nose has chemoreceptors for odors. The mouth has chemoreceptors for taste. The skin has a variety of mechanoreceptors and baroreceptors for touch.
- Psychoactive drugs affect how neurons in the CNS communicate with each other. In this way a psychoactive drug changes how we feel, think, and interact with the world. Medicinal uses of psychoactive drugs include their use as anesthetics, painkillers, and antidepressants.
- For an animation of the neuromuscular junction see http://www.youtube.com/watch?v=ZscXOvDgCmQ.
- Inside the Teenage Brain; how teenage brains are not adult brains yet: http://www.pbs.org/wgbh/pages/frontline

Review Questions

1. How does the body transmit electrical signals?
2. Describe the structure of a neuron.
3. Distinguish between a neuron and a glial cell.
4. Use 1.35 of an action potential to answer the following questions.

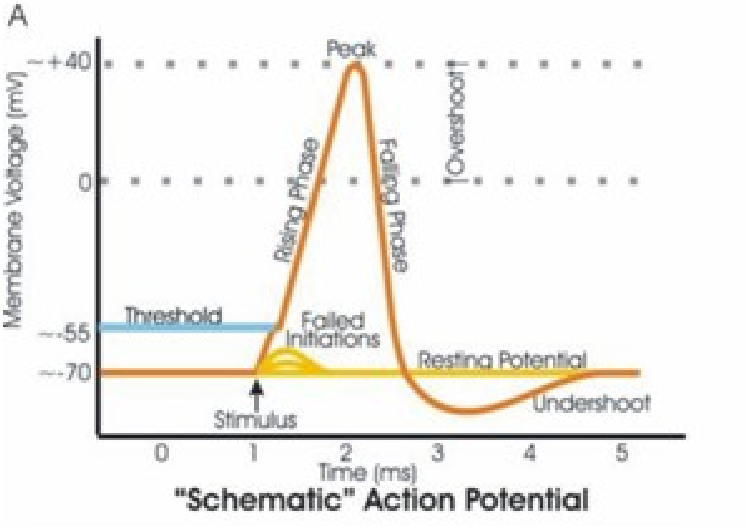

Figure 1.35

What is the membrane potential at the peak (after 2 milliseconds)? Is it positive or negative?

5. What happens to the membrane potential after 5 ms?
6. At the peak point when the membrane potential is 40mV, does the cell have an overall negative

charge or positive charge?
7. Hyperpolarization, which means the cell becomes more negatively charged than it is at resting potential (more negative than -70 mV),can happen as a result of the binding of an inhibitory neurotransmitter to its receptor. Propose what happens to sodium and potassium ions during hyperpolarization.
8. How does voltage relate to the membrane potential?
9. What would happen to a cell if its sodium and potassium pumps failed to work at the end of an action potential?
10. The backflow of a nerve impulse is prevented by the fact that at a chemical synapse, the axon terminal does not have neurotransmitter receptors and dendrites cannot secrete neurotransmitter chemicals. What does this statement tell you about the direction of nerve impulses in neurons?
11. Identify two types of synapses in the nervous system.
12. What is the purpose of the digestive enzymes found in the synaptic cleft?
13. Distinguish a neurotransmitter from a hormone.
14. What is the major function of the central nervous system?
15. Outline the major functions of the cerebral cortex.
16. Use 1.36 of the lobes of the brain to answer the following questions.

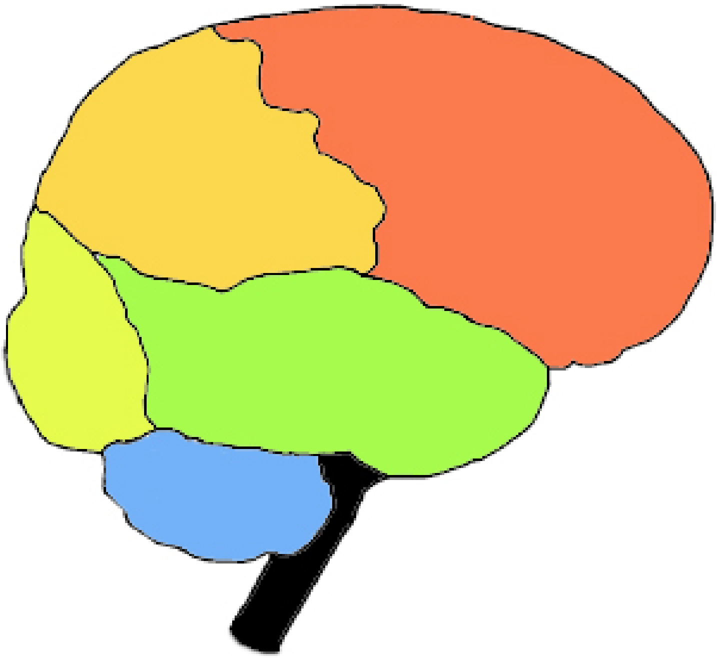

Figure 1.36

What is the name of the blue structure?
17. Identify a sense that is interpreted in the yellow-colored lobe (center left), and name that lobe.
18. Identify the two main divisions of the peripheral nervous system, and describe their roles in the body.
19. What are the two divisions of the autonomic nervous system?
20. Distinguish between the sympathetic and parasympathetic nervous systems.
21. What type of sensory receptors are found in the eyes?
22. Distinguish between rods and cones.
23. Why are taste and smell called the “two chemical senses”?
24. Outline how the ear is important to the sense of body balance.
25. What role does skin have in detecting external stimuli?
26. What kind of effects should a drug have for it to be called *psychoactive*?

27. Identify the main effect of psychoactive drugs on the CNS.
28. How do the effects of a stimulant differ from the effects of a depressant?
29. What is the brain reward system and how is it affected by an addictive drug?
30. How does cocaine affect the brain reward system?
31. Use 1.37 that shows the differences in blood concentration of nicotine over time to answer the following questions.

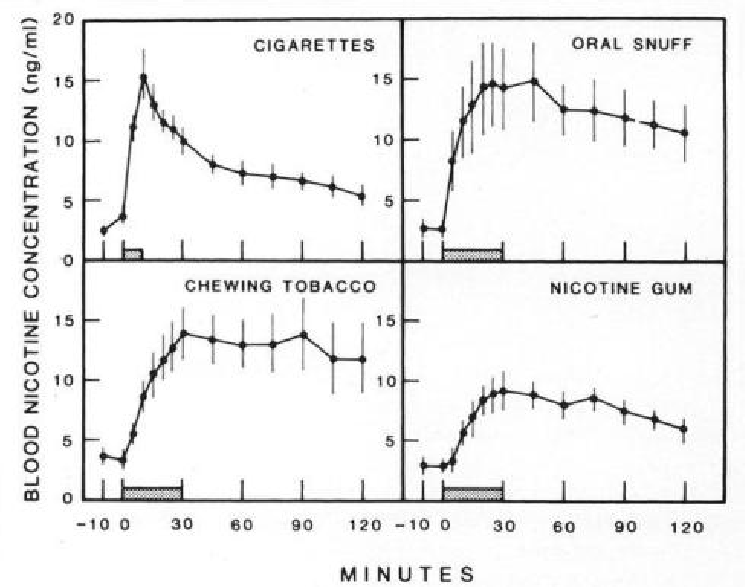

Figure 1.37

32. Review the graph that illustrates the increases in blood-nicotine concentrations from four different forms of tobacco; Cigarettes, oral snuff, chewing tobacco, and nicotine gum. Which of the four forms of nicotine increases blood-nicotine concentration the fastest?
33. Which of the four forms of nicotine increases blood-nicotine concentration the least?
34. Can you tell from this graph whether one form of tobacco is safer than another?

Further Reading / Supplemental Links

- http://training.seer.cancer.gov/module_anatomy/unit5_2_nerve_tissue.html
- http://brainmaps.org/
- http://teens.drugabuse.gov/index.asp
- http://www.nida.nih.gov/scienceofaddiction

Vocabulary

action potential An electrical charge that travels along the membrane of a neuron.

agonists Drugs that increase activity in particular neurotransmitter systems; act by increasing the synthesis of one or more neurotransmitters or reducing its reuptake from the synapses.

antagonists Drugs that reduce neurotransmitter activity; work by interfering with synthesis or blocking postsynaptic receptors so that neurotransmitters cannot bind to them.

astrocytes A type of glial cell in the brain; important for the maturation of neurons and may be involved in repairing damaged nervous tissue.

autonomic nervous system (ANS) The part of the peripheral nervous system that maintains homeostasis in the body; controls such actions as heart rate, digestion, respiration rate, salivation, and perspiration; also called the involuntary nervous system.

axon A long, membrane-bound extension of the cell body that passes the nerve impulse onto the next cell.

axon terminal The end of the axon; the point at which the neuron communicates with the next cell.

brain stem Part of the brain involved with unconscious (autonomic) functions such as breathing, heartbeat, and temperature regulation; contains the midbrain, the pons, and the medulla oblongata.

cerebellum The part of the brain that is involved in coordination and control of body movement.

cerebral cortex The highly-folded outer layer of the cerebrum; controls higher functions, such as consciousness, reasoning, emotions, and language; also controls sensory functions such as touch, taste, smell, and responses to external stimuli.

cerebrum The part of the brain that generally controls conscious functions such as problem-solving and speech.

central nervous system (CNS) Made up of the brain and spinal cord; the brain is the central control of the CNS; the spinal cord carries nerve impulses from the brain to the body and from the body to the brain.

chemical synapse A synapse that uses chemical signaling molecules as messengers.

cochlea A coiled tube within the ear; filled with a watery liquid which moves in response to the vibrations coming from the middle ear through the oval window; as the fluid moves, thousands of mechanoreceptors called hair cells bend, releasing a neurotransmitter.

cone cells Photosensitive cells important to vision; located in the retina; respond to different wavelengths of bright light to initiate a nerve impulse; also responsible for the sharpness of images.

dendrites Extend from the cell body and receive a nerve impulse from another cell.

diencephalons The region of the brain that includes structures such as the thalamus, the hypothalamus, and a portion of the pituitary gland.

dorsal root The ‘‘nerve highway;’’ carries sensory information from sensory receptors in the body to the CNS.

drug Any chemical or biological substance that affects the body’s structure or functions.

drug abuse The repeated use of a drug without advice or guidance of a medical professional, and use for reasons other than for what the drug was originally intended.

electrical synapse Synapse that uses ions as messengers.

endocrine system A system of glands around the body that release chemical signal molecules into the bloodstream.

glial cell Cell that provides a support system for the neurons; also involved in synapse formation.

hallucinogens Psychedelic drugs, such as lysergic acid diethylamide (LSD), phencyclidine (PCP), and ketamine; psychoactive drugs that do not increase or decrease a certain feeling or emotion, but rather they induce experiences, such as sensory distortions and "out-of-body experiences," that are very different from those of ordinary consciousness.

hearing The sense of sound perception that results from the movement of tiny hair fibers in the inner ear.

hypnotics (depressants) Drug that decreases the activity of the central nervous system; slows down brain function and give a drowsy or calm feeling; includes alcohol, codeine, barbiturates, and benzodiazepines.

interneurons Neurons that connect sensory and motor neurons in neural pathways that go through the CNS; also called association or relay neurons.

medicine (or medication) A drug that is taken to cure or reduce the symptoms of an illness.

membrane potential The voltage across a membrane; the basis for the conduction of nerve impulses along the cell membrane of neurons.

midbrain Part of the brain involved with unconscious (autonomic) functions such as breathing, heartbeat, and temperature regulation.

motor division Subdivision of the PNS; carries nerve impulses from the CNS to the muscles, glands and organs of the body; also called the efferent division.

motor neurons Neurons that carry signals from the central nervous system to muscles and glands; sometimes called efferent neurons.

myelin sheath An electrically insulating phospholipid layer; covers the axon; speeds up the transmission of a nerve impulse along the axon.

nerve An enclosed, cable-like bundle of axons.

nervous system A complex network of nervous tissue that sends electrical and chemical signals; includes the central nervous system (CNS) and the peripheral nervous system (PNS) together.

neuromuscular junction A synapse between a neuron and a muscle cell.

neuron The ”conducting” cell that transmits electrical signals; the structural unit of the nervous system.

neurotransmitter Chemical messages which are released at the synapse and pass the ‘‘message” onto the next neuron or other type of cell.

nociceptor A type of pain receptor which responds to potentially damaging stimuli.

Nodes of Ranvier Regularly spaced gaps between the myelin; the only points at which ions can move across the axon membrane, through ion channels.

olfactory receptors The chemoreceptors of smell.

oligodendrocytes Glial cells that supply myelin to neurons of the brain and spinal cord.

parasympathetic division Subdivision of the ANS; controls non-emergency functions such as digestion.

peripheral nervous system (PNS) Made up of the nervous tissue that lies outside the CNS, such as the nerves in the legs, arms, hands, feet and organs of the body.

pinna The folds of cartilage surrounding the outer ear canal; gathers sound waves which are channeled down the auditory canal, a tube-shaped opening of the ear which ends at the tympanic membrane, or eardrum.

psychoactive drug A substance that affects the central nervous system by altering cognitive function.

reflex An automatic (involuntary) action caused by a defined stimulus and carried out through a reflex arc.

resting potential The resting state of the neuron, during which the neuron has an overall negative charge.

reuptake The removal of a neurotransmitter from the synapse by the pre-synaptic neuron; a way of controlling the effect the neurotransmitter has on the post-synaptic cell.

rod cells Photosensitive cells important to vision; located in the retina; highly sensitive to light which allows them to respond in dim light and dark conditions, but, they cannot detect color.

Schwann cells Cells that supply the myelin for neurons that are not part of the brain or spinal cord.

sensory division Subdivision of the PNS; carries sensory information from sensory receptors in the body to the CNS; also known as the afferent division.

sensory neurons Neurons that carry signals from tissues and organs to the central nervous system; sometimes called afferent neurons.

sight (vision) Describes the ability of the brain and eye to detect certain wavelengths of electromagnetic radiation (light), and interpret the image.

sodium-potassium pump Transport protein that removes Na^+ ions from the cell by active transport; also brings K^+ ions into the cell.

somatic nervous system The part of the PNS that is associated with the conscious (voluntary) control of the body through the movement of skeletal muscles and the perception of external stimuli through senses such as touch, hearing, and sight.

spinal cord A thin, tubular bundle of nervous tissue that extends from the medulla oblongata and continues to the lower back; functions as an information superhighway that links the sensory messages from the body to the brain.

stimulant Psychoactive drug, such as cocaine, nicotine, and amphetamine, that increases the activity of the sympathetic nervous system, the central nervous system, or both; generally increase heart rate, blood pressure, and increase the sense of alertness.

sympathetic division Subdivision of the ANS; generally stimulates body systems during emergency situations.

synapse A specialized junction at which neurons communicate with each other.

synaptic cleft Gap between the axon terminal of the presynaptic neuron and the receiving cell.

threshold Level of depolarization the membrane potential has to surpass for the action potential to start.

touch The sense of pressure perception, which is generally felt in the skin.

ventral root Contains axons of motor neurons which carry information away from the CNS to the muscles and glands of the body.

voltage Electrical potential energy that is caused by a separation of opposite charges.

Points to Consider

- The electrical signals of the nervous system move very rapidly along nervous tissue, while the chemical signals of the endocrine system act much more slowly and over a longer period of time. Identify some of advantages to having two different speeds for communications in the body.
- Identify ways that psychoactive drug abuse may negatively affect organ systems other than the nervous system.
- The cerebral cortex controls functions such as consciousness, reasoning, emotions, and language. The brain stem is the lower part of the brain that is involved with unconscious, autonomic functions. Consider why consciousness and reasoning are called “higher functions” in relation to the “lower functions” of breathing and heartbeat.

1.2 The Endocrine System

Lesson Objectives

- Identify the main functions of the endocrine system.
- Identify the structures that produce hormones.
- Outline how hormones affect certain cells and not others.
- Describe two ways that hormones influence the function of cells.
- Identify the two glands that serve as the major control centers of the endocrine system.
- Identify the effects of adrenal hormones on the body.
- Examine the importance of the islets of Langerhans.
- Outline the role of the sex hormones in reproduction.
- Identify non-endocrine organs that secrete hormones.
- Examine how feedback mechanisms control hormone levels and body functions.
- Identify the role of hormone antagonists in the control of substances in the body.
- Identify two medical uses of hormones.

Introduction

The **endocrine system** is a system of organs that releases chemical message molecules, called hormones, into the blood. Unlike the nervous system whose action helps the body react immediately to change, such as quickly jumping out of the way of an oncoming cyclist, the endocrine system controls changes that happen to the body over a long period of time; from minutes, hours, to years of change. The two systems work closely together to help us respond to our environment, such as the rollercoaster ride shown in **Figure** 1.38. The endocrine system is important in controlling metabolism, growth and development, reproduction, and salt, water and nutrient balance of blood and other tissues (osmoregulation).

Figure 1.38: What an adrenaline rush! The excitement that the people on this rollercoaster are feeling is a good example of how the nervous and endocrine systems work together. Nerve impulses from the sympathetic nervous system cause the adrenal medulla to release the hormone adrenaline into the bloodstream. Adrenaline causes the racing heart, sweaty palms, and feeling of alertness that together are called the &quot;fight or flight&quot; response.

Function of the Endocrine System

The nervous system uses nerves to conduct electrical and chemical information around the body, while the endocrine system uses blood vessels to carry chemical information. You can think of the nervous system as being similar to the electrical system in a house. Flicking on a light switch is similar to initiating an action potential in a nerve, and it has an almost immediate result: the light bulb illuminates. The endocrine system on the other hand is more like starting up an oil or gas powered water-heating system. You flick on the switch to heat water up for a bath, but it takes a certain length of time for the result to occur: hot water.

Organs of the Endocrine System

The endocrine system is made up of many glands that are located in different areas of the body. **Hormones** are chemical messenger molecules that are made by cells in one part of the body and cause changes in cells in another part of the body. Hormones regulate the many and varied functions that keep you alive.

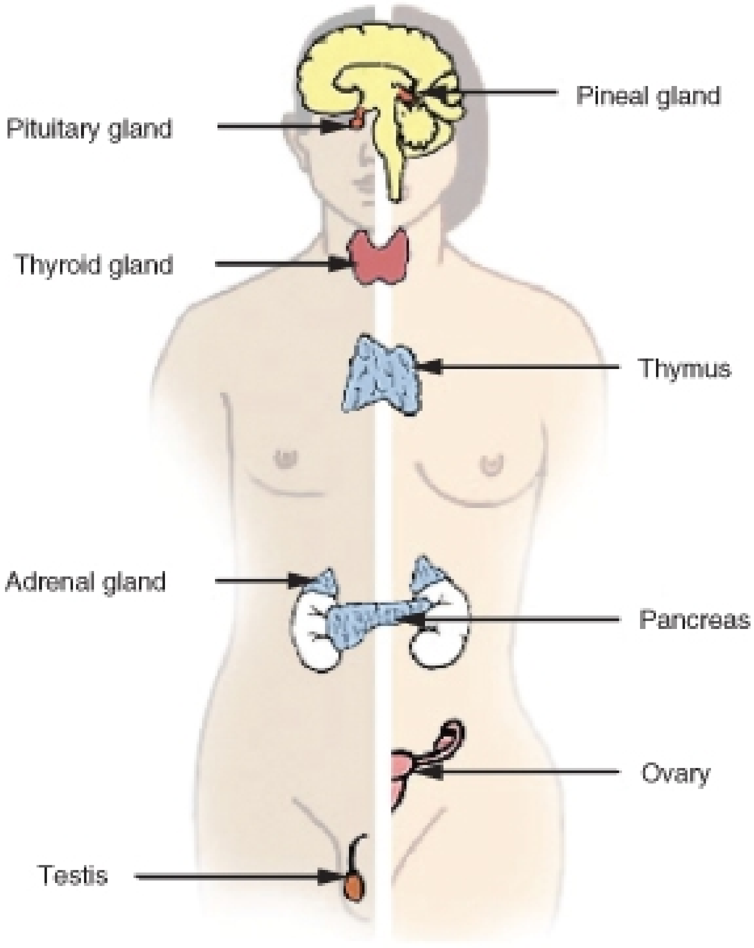

Figure 1.39: The major organs of the endocrine system.

Hormones are made and secreted by cells in endocrine glands. **Endocrine glands** are ductless organs that secrete hormones directly into the blood or the fluid surrounding a cell rather than through a duct. The primary function of an endocrine gland is to make and secrete hormones. The endocrine glands collectively make up the **endocrine system**. The major glands of the endocrine system and their functions are shown in **Figure** 1.39. Many other organs, such as the stomach, heart, and kidneys secrete hormones and are considered to be part of the endocrine system.

Exocrine glands are organs that secrete their products into ducts (they are duct glands). They are similar to endocrine glands in that they secrete substances, but they do not secrete hormones. Instead they secrete products such as water, mucus, enzymes, and other proteins through ducts to specific locations inside and outside the body. For example, sweat glands secrete sweat onto the skin and salivary glands secrete saliva into the mouth. The reason we are discussing exocrine glands in a chapter about hormones is because some endocrine glands, such as the pancreas, are also exocrine glands. Ducts in the pancreas secrete fat-digesting enzymes into the intestines. The secretion of the enzymes from the pancreas is controlled by hormones that are made by certain stomach cells.

Hormones

The body produces many different hormones, but each hormone is very specific for its target cells. A **target cell** is the cell on which a hormone has an effect. Target cells are affected by hormones because they have receptor proteins that are specific to the hormone. Hormones will travel through the bloodstream until they find a target cell with the specific receptors to which they can bind. When a hormone binds to a receptor, it causes a change within the cell.

There are two main types of hormones, and a group of hormone-like substances:

- **Amino Acid-Based Hormones**

Amino acid-based hormones are made of amino acids. Some amino acid-based hormones are made of a few amino acids and are simple in structure while others are made of hundreds of amino acids and are very large. These hormones are not fat-soluble and therefore cannot diffuse through the plasma membrane of their target cell. They usually bind to receptors that are found on the cell membrane.

- **Cholesterol-Based Hormones**

Cholesterol-based hormones are made of lipids such as phospholipids and cholesterol. Hormones from this group are also called steroid hormones. Steroid hormones are fat soluble and are able to diffuse through the plasma membrane. Steroid hormone receptors are found within the cell cytosol and nucleus.

- **Hormone-like Substances**

The term hormone-like substances refers to a group of signaling molecules that are derived from certain types of fatty acids and proteins. Two examples of these substances are prostaglandins and neuropeptides. These substances do not travel around the body in blood as hormones do and tend to be broken down quickly. As a result, the effects of hormone-like substances are localized in the tissue in which it they are produced. For example, **prostaglandins**, which are made from essential fatty acids, are produced by most cells in the body. Prostaglandins have many different effects such as causing constriction or dilation of blood vessels but they are all are localized within the target cells and tissues. **Neuropeptides** are signaling peptides found in nervous tissue. Neuropeptides have many effects on nerve cells. For example, they can affect gene expression, local blood flow, and the shape of glial cells. Some neuropeptides such as endorphins and oxytocin have effects on non-nerve cells and are called hormones. Both signaling molecules have an effect on behavior. Among other things, endorphins are involved in pain perception and oxytocin is involved in social bonding and maternal behavior.

The cells that make hormones are usually specialized for the job, and are found within a particular endocrine gland, for example the thyroid gland, the ovaries, or the testes. Hormones may exit their cell of origin by exocytosis or another type of membrane transport. Typically cells that respond to a particular hormone may be one of several cell types that are found in different tissues throughout the body. Such is the case for insulin, which triggers a great number of physical effects. Different tissue types may also respond differently to the same hormonal signal. Because of this, hormonal signaling is a very complex process.

Hormone Receptors

Cells that respond to hormones have two properties in common: they have receptors that are very specific for certain hormones, and those receptors are joined with processes that control the metabolism of the target cells. There are two main ways that receptor-bound hormones activate processes within cells, depending on whether the hormone can pass across the membrane (steroid hormones are fat-soluble), or cannot pass through the membrane (most amino acid based hormones are water soluble).

- **Second Messenger System**

A water-soluble hormone molecule does not enter the cell, instead it binds to the membrane-bound receptor molecule, which triggers changes within the cell. These changes are activated by second messenger molecules.

- **Direct Gene Activation**

A fat-soluble hormone diffuses across the membrane and binds to the receptor within the cytosol or nucleus. The hormone-receptor complex then acts as a transcription factor that affects gene expression.

The two different ways that hormones can activate cells are discussed here, using the amino-acid based hormone glucagon and the steroid hormone cortisol as examples.

Action of Glucagon: A Second Messenger System

The majority of amino-acid based hormones, such as glucagon, bind to membrane-bound receptors. The binding of the hormone triggers a **signal transduction pathway**, a process of molecular changes that turns the hormone's extracellular signal into an intracellular response. Activation of these receptors by hormones (the first messengers) leads to the intracellular production of second messengers as part of the signal transduction pathway. A **second messenger** is a small molecule that starts a change inside a cell in response to the binding of a specific signal to a receptor protein. Some second messenger molecules include small molecules such as cyclic AMP (cAMP), cyclic GMP (cGMP), and calcium ions (Ca^{2+}).

Glucagon is an important hormone involved in carbohydrate metabolism. It is released when the glucose level in the blood is low which causes the liver to change stored glycogen into glucose and release it into the bloodstream. Glucagon is released by the pancreas and circulates in the blood until it binds to a glucagon receptor, a G protein-linked receptor, found in the plasma membrane of liver cells. The binding of glucagon (first messenger) changes the shape of the receptor, which then activates a G protein. The G-protein is an enzyme that in turn activates the next enzyme in the cascade, the second messenger; adenylate cyclase. Adenylate cyclase produces cAMP which activates another enzyme, which in turn activates another enzyme, and so on. The end result is an enzyme that breaks apart the glycogen molecule in the liver cell to release glucose molecules into the blood. The signal transduction pathway, a type of enzyme "domino-effect" inside the cell, allows a small amount of hormone to have a large effect on the cell or tissue. To learn more about second messenger systems, refer to the *Cell Structure and Function* chapter.

Action of Cortisol: A Direct Gene Activation

Steroid hormones diffuse through cell membrane and bind to receptors in the cytosol or the nucleus of the cell. The receptor-hormone complex acts as a transcription factor that affects gene expression.

Cortisol is a steroid hormone produced by the adrenal glands. It is often called the "stress hormone" as it is involved in the body's response to stress. It increases blood pressure, blood sugar levels and has an immunosuppressive action. Cortisol crosses the cell membrane and binds to a steroid receptor in the cytoplasm. The cortisol-receptor complex then enters the nucleus of the cell and binds to DNA, where it activates or deactivates gene transcription. The gene that is activated or deactivated depends on the cell type.

Effects of Hormones

The effects of hormones vary widely, and certain hormones, called tropic hormones (or tropins), regulate the production and release of other hormones. Many of the responses to hormones regulate the metabolic activity of an organ or tissue.

Other effects of hormones can include:

- Stimulation or inhibition of growth
- Induction or suppression of programmed cell death (apoptosis)
- Activation or inhibition of the immune system
- Regulation of metabolism
- Preparation for a new activity (e.g., fighting, fleeing, mating)
- Preparation for a new phase of life, for example puberty, caring for offspring, or menopause
- Control of the reproductive cycle

You will learn more about the effects of certain hormones as we examine some of the endocrine glands individually.

Hypothalamus and Pituitary Gland

The **hypothalamus** links the nervous system to the endocrine system by the pituitary gland. The hypothalamus is located below the thalamus, just above the brain stem. It is found in all mammalian brains, including humans. The human hypothalamus is about the size of an almond; its position in the brain is shown in **Figure** 1.40.

The hypothalamus is a very complex area of the brain, and even small numbers of nerve cells within it are involved in many different functions. The hypothalamus coordinates many seasonal and circadian rhythms, complex homeostatic mechanisms, and the autonomic nervous system (ANS). A **circadian rhythm** is a roughly-24-hour cycle in the biological processes carried out within organisms, including plants, animals, fungi and certain bacteria. The ANS controls activities such as body temperature, hunger, and thirst. The hypothalamus must therefore respond to many different signals, some of which are from outside and some from inside the body. Thus, the hypothalamus is connected with many parts of the CNS, including the brainstem, the olfactory bulbs, and the cerebral cortex.

The hypothalamus produces hormones that are stored in the pituitary gland. For example, oxytocin and antidiuretic hormone (ADH) are made by nerve cells in the hypothalamus, and are stored in the pituitary prior to their release into the blood. In addition to influencing maternal behavior, oxytocin is involved in controlling circadian homeostasis, such as a person's body temperature, activity level, and wakefulness

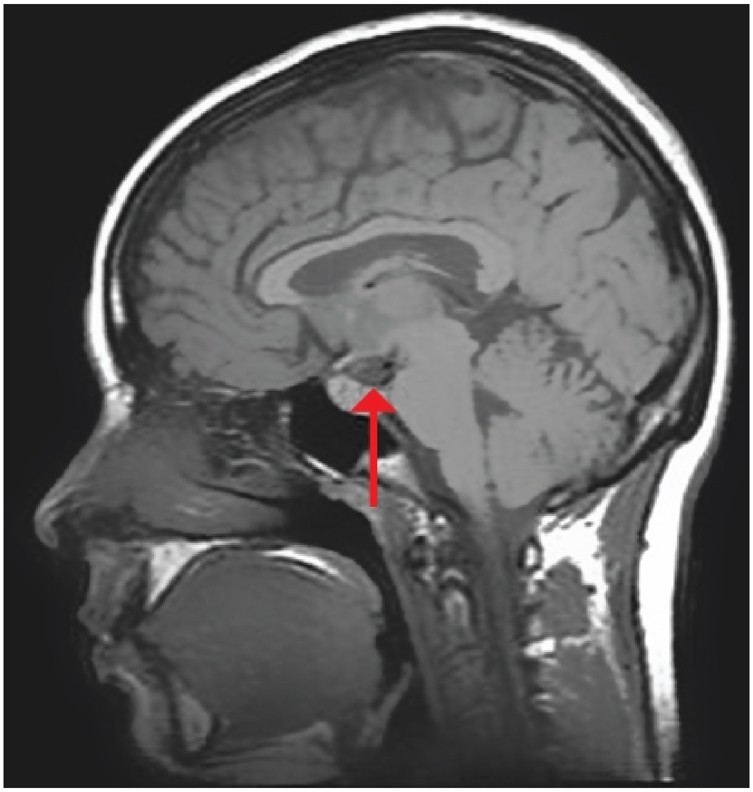

Figure 1.40: The hypothalamus is here. The red arrow shows the position of the hypothalamus in the brain.

at different times of the day. Antidiuretic hormone (ADH) is released when the body is low on water; it causes the kidneys to conserve water by concentrating the urine and reducing urine volume. It also raises blood pressure by causing blood vessels to constrict.

Pituitary Gland

The **pituitary gland** is about the size of a pea and is attached the hypothalamus by a thin stalk at the base of the brain, shown in **Figure** 1.41. The pituitary gland secretes hormones that regulate homeostasis. It also secretes hormones that stimulate other endocrine glands, called tropic hormones.

The **anterior pituitary**, or front lobe, makes many important hormones, which are listed in **Table** 1.5. The **posterior pituitary**, or rear lobe, releases two hormones, oxytocin and antidiuretic hormone (ADH) that are made by nerve cells in the hypothalamus. These hormones are transported down the nerve cell's axons to the posterior pituitary where they are stored until needed.

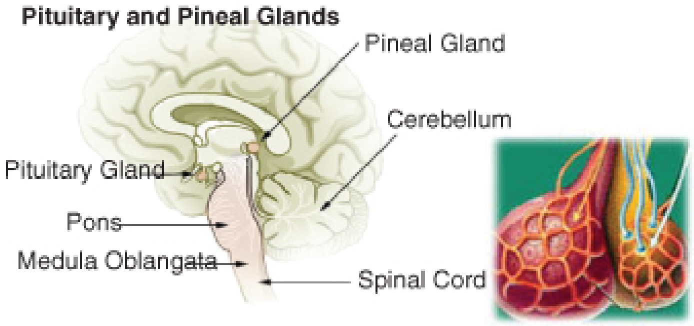

Figure 1.41: The position of the pituitary in the brain. A close-up of the anterior and posterior pituitary gland can be seen at right. The orange vessels are the capillary system that comes from the hypothalamus and carries hormones to the anterior pituitary (red) for storage. The blue vessels on the posterior pituitary come from the neurosecretory cells in the hypothalamus.

Table 1.5: **Pituitary Hormones**

Location	Hormone	Target	Function
Anterior Pituitary	Adrenocorticotropic hormone (ACTH) Thyroid-stimulating hormone (TSH) Growth hormone (GH) Follicle stimulating hormone (FSH) Leutinizing hormone (LH) Prolactin (PRL)	Adrenal Gland Thyroid Gland Body cells Ovaries, Testes (Gonads) Ovaries, Testes Ovaries, mammary glands	Stimulates adrenal cortex Stimulates thyroid Growth hormone Stimulates production of ovarian follicles in females, sperm production in males Causes ovulation in females Causes milk secretion
Posterior Pituitary	Anti diuretic hormone (vasopressin) Oxytocin	Kidneys or Arterioles uterus, mammary glands	Promotes water reabsorption in kidneys, raises blood pressure Causes uterus to contract in childbirth, stimulates milk flow

Most of these hormones are released from the anterior pituitary under the influence of hormones from the hypothalamus. The hypothalamus hormones travel to the anterior lobe down a special capillary system that surrounds the pituitary.

Oxytocin is the only pituitary hormone to create a positive feedback loop. For example, during the labor and delivery process, when the cervix dilates the uterus contracts. Uterine contractions stimulate the release of oxytocin from the posterior pituitary, which in turn increases uterine contractions. This positive feedback loop continues until the baby is born.

Other Endocrine Glands

Thyroid and Parathyroid Glands

The **thyroid** is one of the largest endocrine glands in the body. This butterfly-shaped gland is found in the neck, wrapped around the trachea, as shown in **Figure** 1.42. The hormones released by the thyroid control how quickly the body uses energy, makes proteins, and how sensitive the body should be to other hormones. The thyroid is controlled by the hypothalamus and pituitary. Thyroid hormone generally controls the pace

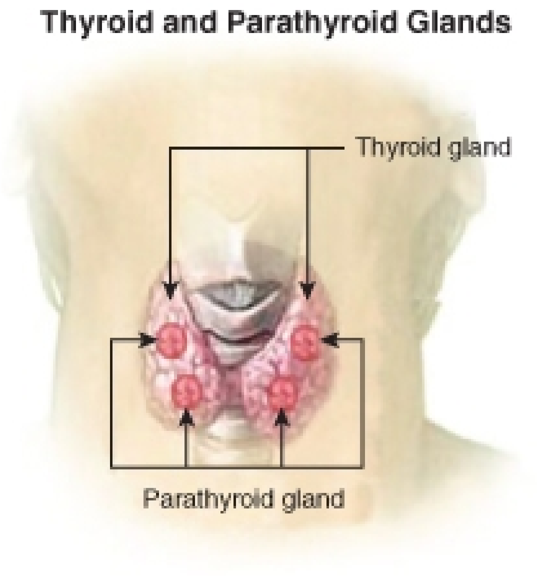

Figure 1.42: The position of the thyroid and parathyroid glands. A person can have more than four parathyroid glands.

thyroid gland. The addition of small amounts of iodine to mass produced foods, such as table salt, has helped reduce the occurrence of iodine-deficiency in developed countries. The thyroid also produces the hormone calcitonin, which plays a role in calcium homeostasis. The hormones secreted by the thyroid are listed in **Table** 1.6.

Table 1.6: **Hormones Secreted by the Thyroid and Parathyroid Glands**

Location	Hormone	Target	Function
Thyroid	Triiodothyroine (T3) Thyroxine (T4) Calcitonin	Body Cells Bone cells	Increase metabolic rate, stimulates mental and physical growth Increases calcium absorption by bones, lowers blood calcium level
Parathyroid	Parathyroid hormone (PTH)	Cells of the bone, kidney, and intestines	Regulates blood calcium levels

Parathyroid Glands

The parathyroid glands are usually located behind the thyroid gland, but they are visible in **Figure** 1.42. Parathyroid hormone (PTH), maintains blood calcium levels within a narrow range, so that the nervous and muscular systems can work properly. When blood calcium levels drop below a certain point, calcium-sensing receptors in the parathyroid gland release the hormone parathyroid hormone (PTH) into the blood. PTH has effects that are opposite to the action of calcitonin. It increases blood calcium levels by stimulating certain bone cells to break down bone and release calcium. It also increases gastrointestinal calcium absorption by activating vitamin D, and promotes calcium uptake by the kidneys. The hormones secreted by the parathyroid glands are listed in **Table** 1.6.

Pineal Gland

Figure 1.43: Very little is currently known about the role of melatonin, but scientists do know that it is involved in sleep cycles. It is produced by the pineal gland, the retina and the intestines. Production of melatonin by the pineal gland is influenced of by the hypothalamus which receives information from the retina about the daily pattern of light and darkness.

where it is stored as glycogen, a polysaccharide. **Glucagon** is produced by alpha cells and stimulates liver cells to break down stores of glycogen into glucose which is then released into the blood. An alpha cell is another type of endocrine cell that is found within the islets of Langerhans. The hormones secreted by the pancreas are listed in **Table** 1.7.

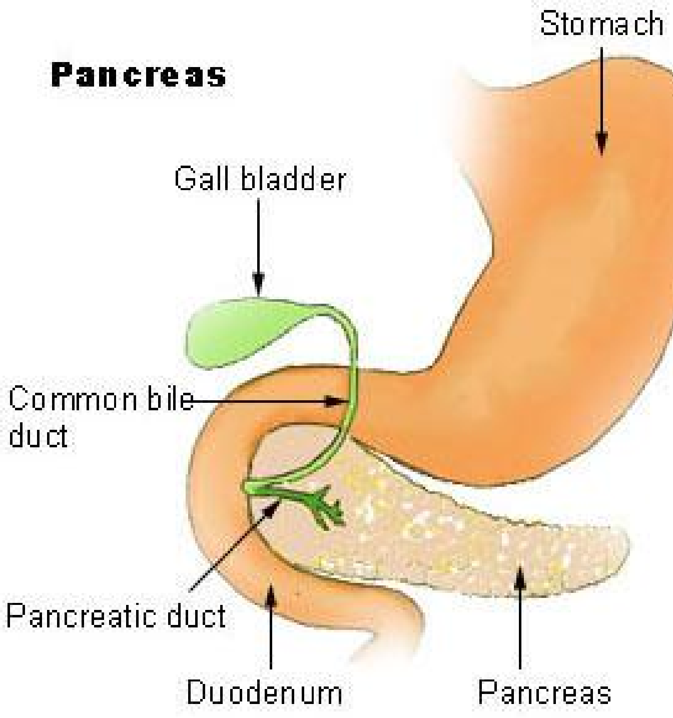

Figure 1.44: The location of the pancreas in relation to the stomach and gall bladder. The hormone-producing Islet cells a found in groups throughout the pancreas.

Table 1.7: **Hormones Secreted by the Pancreas**

	Hormone	Effects
	Insulin Glucagon Amylin Somatostatin (inhibitory hormone) Ghrelin	Reduces blood glucose concentration Raises blood glucose concentration Suppresses glucagons secretion Suppress the release of insulin, glucagon, and pancreatic enzymes Stimulates appetite

Adrenal Glands

An adrenal gland is located above each of the kidneys, as shown in **Figure** 1.46. Each adrenal gland is separated into two structures, the adrenal medulla, which is the center of the gland, and the adrenal cortex,

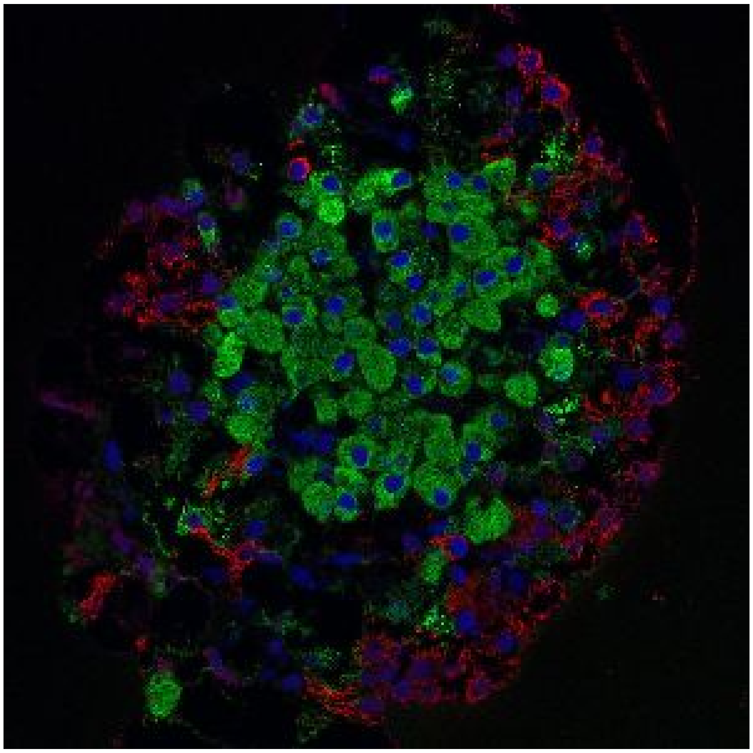

Figure 1.45: Micrograph of an islet of Langerhans isolated from a rat pancreas. Each islet in a human pancreas contains approximately 1000 cells and is 50 to 500 micrometers in diameter. Cell nuclei are stained blue, insulin-producing beta cells are green, and glucagon-producing alpha cells are red.

which is the outer layer. The medulla and the cortex work as two separate endocrine glands.

The **adrenal medulla** is the core of the adrenal gland, and is surrounded by the adrenal cortex. Secretion of hormones from the medulla is controlled by the sympathetic nervous system. The cells of the medulla are the body's main source of the hormones **adrenaline** (epinephrine) and **noradrenaline** (norepinephrine). These hormones are part of the fight-or-flight response initiated by the sympathetic nervous system. The hormone boosts the supply of oxygen and glucose to the brain and muscles, while suppressing other non-emergency bodily processes, such as digestion.

The **adrenal cortex** is the site of steroid hormone synthesis. Some cells make cortisol, while other cells make androgens such as testosterone. Other cells of the cortex regulate water and electrolyte concentrations by secreting aldosterone, which helps to regulate blood pressure. In contrast to the medulla that is controlled directly by the nervous system, the cortex is regulated by hormones secreted by the pituitary gland and hypothalamus.

Cortisol is an important steroid hormone that is often called the ”stress hormone” as it is involved in the response to stress, and is involved in restoring homeostasis after a stressful event, such as the (good) stress caused by running around a soccer field [football pitch (for non-American-English speakers)], shown in **Figure** 1.47. Cortisol increases blood pressure, blood sugar levels and has an immunosuppressive action. Long-term stress causes prolonged cortisol secretion, hyperglycemia, and weakening of the immune system. Excess levels of cortisol in the blood result in Cushing's syndrome, symptoms of which include rapid weight gain, a round face, excess sweating, and thinning of the skin and mucous membranes.

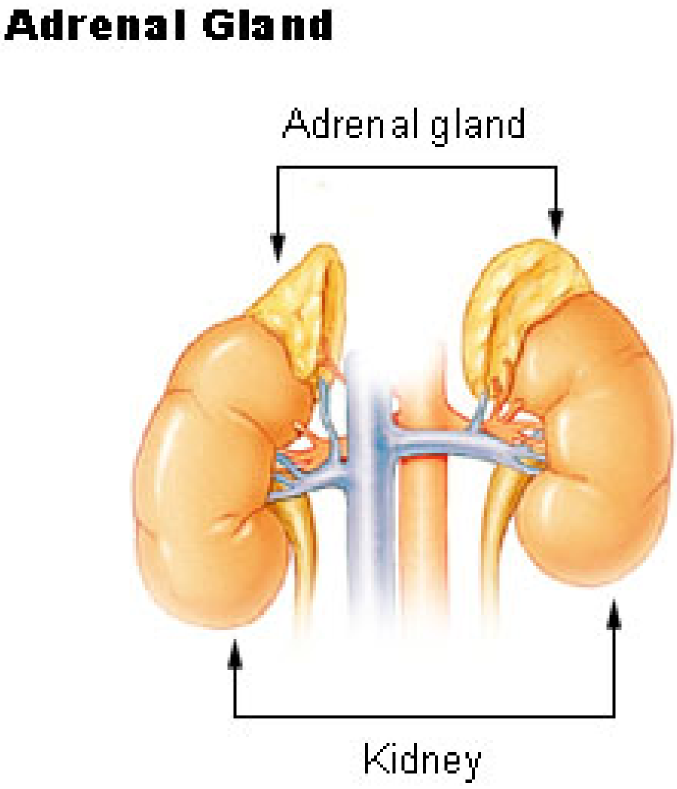

Figure 1.46: The location of the adrenal glands, above the kidneys.

Figure 1.47: Regular activity through sport is a good way of allowing your body to respond naturally to its stress hormones, which prepare the body for quick movements or prolonged activity.

Table 1.8: **Hormones of the Adrenal Glands**

Location	Hormone	Function
Adrenal cortex		
	Mineralcorticoids (such as aldosterone)	Regulate sodium reabsorption and potassium elimination in the kidneys
	Glucocortocoids (such as cortisol)	Depress immune response, provide stress resistance, helps in fat, protein and carbohydrate metabolism
	Gonadotropins	Stimulates releases of sex hormones that develop sexual characteristics of males and females
Adrenal medulla		
	Epinephrine (adrenaline)	"Fight or flight" hormone, plays central role in short-term response to stress, increases heart rate and supply of blood and oxygen to the brain
	Norepinephrine (noradrenaline)	Increases alertness, physical effect similar to epinephrine

Epinephrine, also called **adrenaline**, is a "fight or flight" hormone which is released from the adrenal medulla when stimulated by the sympathetic nervous system. Epinephrine plays a central role in the short-term stress reaction—the body's response to threatening, exciting, or environmental stressors such as high noise levels or bright light. When secreted into the bloodstream, it binds to multiple receptors and has many effects throughout the body. Epinephrine increases heart rate, dilates the pupils, and constricts blood vessels in the skin and gut while dilating arterioles in leg muscles. It increases the blood sugar level, and at the same time begins the breakdown of lipids in fat cells. It also "turns down" non-emergency bodily processes such as digestion. Similar to other stress hormones, such as cortisol, epinephrine depresses the immune system.

Stress also releases norepinephrine in the brain. **Norepinephrine** has similar actions in the body as adrenaline, such as increasing blood pressure. Norepinephrine is also psychoactive because it affects alertness, which would be helpful for studying as shown in **Figure** 1.48. The hormones secreted by the adrenal cortex and medulla are listed in **Table** 1.8.

Gonads

The ovaries of females and the testes of males are the gamete producing organs, or **gonads**. Ovaries in females are homologous to testes in males. In addition to producing gametes, an exocrine action, the gonads are endocrine glands that produce steroid sex hormones. **Sex hormones** are responsible for the secondary sex characteristics that develop at puberty. **Puberty** is the process of physical changes during

Figure 1.48: Thinking about an upcoming exam can cause your adrenal glands to produce adrenaline (epinephrine). Your body

which the sex organs mature and a person become capable of reproducing. During puberty, among other changes, males begin producing sperm and females begin menstrual cycles.

Luteinizing hormone (LH) and *follicle stimulating hormone* (FSH), which are both secreted by the pituitary gland, are called gonadotropes because they are tropic hormones of the gonads. Recall that tropic hormones trigger the production of hormones in other endocrine glands. The secretion of LH and FSH are, in turn, controlled by gonadotropin-releasing hormone for the hypothalamus. Those pulses, in turn, are subject to the estrogen feedback from the gonads.

In males LH triggers the production of sex hormones called **androgens** in the testes. The main androgen produced by the testes is **testosterone**. Testosterone causes an increase in skeletal muscle mass and bone density and is also responsible for the secondary sex characteristics of males such as facial hair, shown in **Figure** 1.49. The testes also produce small amounts of estrogen in the form of estradiol, which is believed to be important for sperm formation. On average, the human adult male body produces about eight to ten times more testosterone than an adult female body.

Table 1.9: **Hormones Produced by Gonads**

Organ	Hormone	Target	Function
Ovaries	Estrogen	Bone cells, cells of sex organs	Promotes growth and development of female sex organs Maintains Uterine lining
Testes	Progesterone Testosterone	Bone cells, muscle cells, cells of sex organ	Stimulates growth and development of male sex organs and sex drive

In females a rise in LH concentration triggers the production of estrogen and progesterone by the ovaries. Estrogen causes the release of an egg from the ovaries and progesterone prepares the uterus for a possible implantation by a fertilized egg. The placenta is an endocrine gland of pregnancy because it secretes the hormones estrogen, human chorionic gonadatropin, and progesterone which are important for maintaining a pregnancy, shown in **Figure** 1.50. The hormones secreted by the male and female gonads are listed in **Table** 1.9.

Other Hormone-Producing Tissues and Organs

Figure 1.49: The male hormone testosterone stimulates the growth of facial hair. Many men develop facial hair in the later years of puberty, usually between the ages of 15 to 18 years. The amount of facial hair on a man's face varies between individuals, and also between ethnic groups. For example, men from many East Asian or West African backgrounds typically have much less facial hair than those of Western European, Middle Eastern, or South Asian descent.

Figure 1.50: Maintaining correct hormone levels (especially progesterone), throughout pregnancy is important for carrying a pregnancy to full term.

the effect of hormones is also controlled by hormone antagonists. In these ways, the concentration of hormones and their products is kept within a narrow range so as to maintain homeostasis.

A **feedback control mechanism**, or a **feedback loop**, is a signaling system in which a product or effect of the system controls an earlier part of the system, either by shutting the process down or speeding it up. Most feedback mechanisms of the body are negative, only a few are positive. **Hormone antagonists** and **hormone receptor antagonists** are hormones or other molecules that block the action of hormones, and are also used by the body to control the action of hormones.

Negative Feedback

Negative feedback is a reaction in which the system responds in such a way as to reverse the direction of change. Since this tends to keep things constant, it allows for a process to return from a state of imbalance back to a homeostatic equilibrium.

A common, non-biological example of negative feedback happens in a home heating system. When you are home, you set your thermostat to 21 ° C (about 70 ° F), which is the **set point**. The thermometer in the thermostat monitors the room temperature and will sense when the temperature drops below the 21 ° C set point (the stimulus). The thermometer will then send a message to the thermostat (control center), which in turn sends a message to the furnace to switch on and heat up the room. When the room temperature returns to the set temperature, the thermostat shuts the furnace off. In this home-heating example, the increase in air temperature is the negative feedback that results in the furnace being shut off. In this way a set room temperature of 21 ° C (within a degree or two) is maintained.

An example of negative feedback in the body is the control of blood-glucose concentrations by insulin. A higher amount of glucose in the blood (the stimulus), signals the beta cells of the pancreas to release insulin into the blood. Hormone concentration alone cannot trigger a negative feedback mechanism, negative feedback is instead triggered by an overproduction of the effect of the hormone, such as the lowering of blood glucose concentration (the effect), which causes a decrease in the secretion of insulin by the pancreas.

Negative Feedback: Regulation of Thyroid Hormones

The thyroid hormones thyroxine (T4) and triiodothyronine (T3) regulate the rate of metabolism. The production of T4 and T3 is regulated by a thyroid-stimulating hormone (TSH), which is released by the anterior pituitary. The thyroid and the TSH-producing cells of the anterior pituitary form a negative feedback loop, as shown in **Figure** 1.51.

Thyroid-stimulating hormone production is decreased when the T4 levels are high, and when TSH levels are high, T4 production is decreased. The production and secretion of TSH is in turn controlled by thyrotropin-releasing hormone (TRH), which is produced by the hypothalamus. The rate of TRH secretion is increased in situations such as cold temperature because increasing the metabolic rate would generate more heat. Increased levels of T4 and T3 in the blood cause a reduction in TRH secretion. Among other things, TSH secretion is reduced by high levels of thyroid hormones, as well as the antagonistic hormone somatostatin. These feedback loops keep the concentration of thyroid hormones within a narrow range of concentrations.

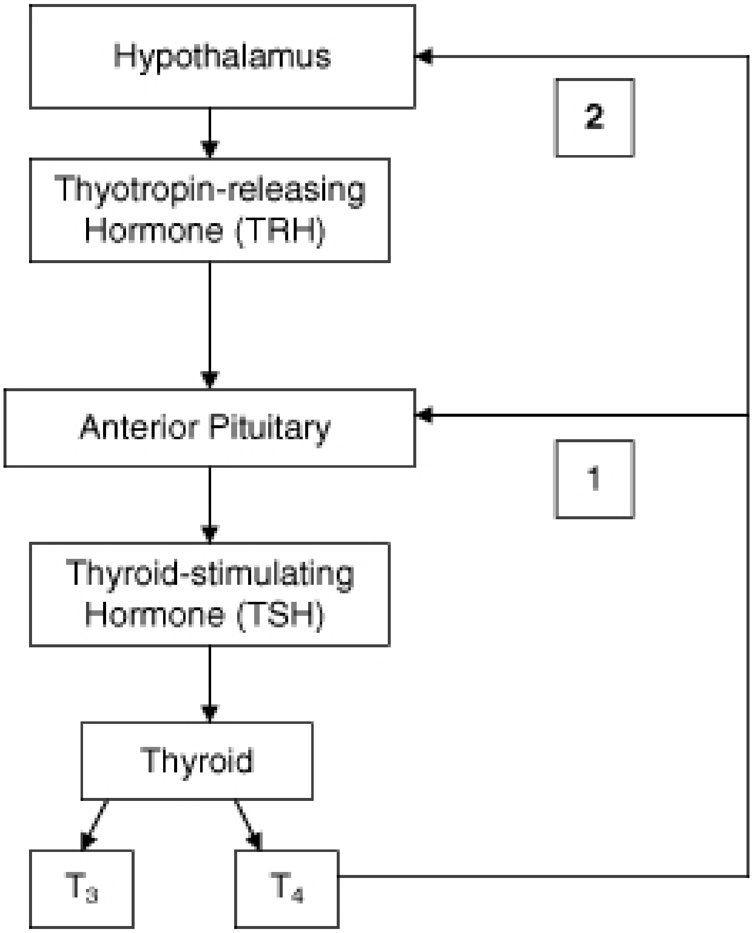
Hypothalamus
2
Thyotropin-releasing Hormone (TRH)
Anterior Pituitary
1
Thyroid-stimulating Hormone (TSH)
Thyroid
T_3
T_4

Figure 1.51: Two negative feedback loops exist in the control of thyroid hormone secretion. (1) shows the loop between the TSH-producing cells of the anterior pituitary and the thyroid. Increased levels of T4 and T3 in the blood cause a reduction in TSH secretion. (2) shows that increased levels of T4 and T3 in the blood cause a reduction in TRH secretion.

Positive Feedback

Positive feedback is a reaction in which the system responds in such a way as to speed up the direction of change. Positive feedback mechanisms are not as common as negative feedback mechanisms because they cause an increase in the initial signal, which would tend to knock many systems out of balance. Take for example, the analogy of the home heating system. If this system were to work on a positive feedback loop, the furnace would not switch off when the temperature reached the set point of 21 ° C. Instead, it would keep going and heat the room indefinitely.

An example of a positive feedback mechanism is milk production by a mother for her baby, as shown in **Figure** 1.52. As the baby suckles, nerve messages from the mammary glands cause the hormone prolactin, to be secreted by the mother's pituitary gland. The more the baby suckles, the more prolactin is released, which stimulates further milk production by the mother's mammary glands. In this case, a negative feedback loop would be unhelpful because the more the baby nursed, the less milk would be produced. Another example of a positive feedback loop is the blood-clotting cascade that happens after a blood vessel is cut.

Figure 1.52: Production of breast milk is controlled by a positive feedback mechanism.

Hormone Antagonists

Many hormones work with hormone antagonists to control the concentrations of substances in the body. The hormones have opposite actions on the body and so are called **antagonistic**.

Insulin and glucagon make up an antagonistic hormone pair. The action of insulin is opposite that of glucagon. For example, your blood glucose concentration rises sharply after you eat food that contains simple carbohydrates, such as the blueberry muffins shown in **Figure** 1.53. The increase in blood glucose level stimulates beta cells in the pancreas to release insulin into blood. In response to signals by insulin most body cells take up glucose, which removes it from the blood, and the blood glucose concentration returns to the set point. Later, you have missed eating lunch, you are hungry and feel a little light-headed. Your blood glucose concentration has dropped below the set point, which causes the release of glucagon from the pancreas. Glucagon causes the release of glucose from liver cells, which increases your blood-glucose concentration. If glucagon did not do its job correctly, your blood glucose concentration would continue to drop, and you would develop hypoglycemia (low blood sugar). This antagonistic relationship between the two hormones helps to maintain the narrow range of blood glucose concentration.

Figure 1.53: Insulin and glucagon work as an antagonistic pair to keep your blood glucose concentration within a narrow range even after you eat food containing carbohydrates, such as a muffin.

The actions of growth hormone releasing hormone (GHRH) are opposed by another hypothalamic hormone, somatostatin, also known as "growth-hormone-inhibiting hormone" (GHIH). Somatostatin and GHRH are secreted alternatively by the hypothalamus, which causes an increase and decrease in the secretion of growth hormone (GH) by the pituitary.

Many endocrine glands also work together as a group to control body processes. The major endocrine glands coordinate the control of various regulatory systems, such as metabolism, osmoregulation, and reproduction. Many individual glands are directly controlled by the nervous system, and all are in some way controlled by the pituitary and hypothalamus. Some of these glands and their hormone products are listed in **Table** 1.10.

Table 1.10: **Coordination of the Endocrine Glands in the Control of Body Systems**

Function	Organ or Glands	Hormones	Nervous System Control
Control of the Endocrine System	Hypothalamus Pituitary Gland	TSH, FSH, LH, GH, prolactin (PRL) Adrenocorticotropic hormone (ACTH)	ANS (sympathetic and parasympathetic nervous system)

Table 1.10: (continued)

Function	Organ or Glands	Hormones	Nervous System Control
Regulation of Metabolism	Thyroid Gland Parathyroid Glands Pancreas Pineal Gland Liver	T_3 and T_4 Parathyroid hormone Insulin Glucagon Melatonin	ANS (sympathetic and parasympathetic nervous system)
Response to Stress	Adrenal Glands	Epinepherine, norepinepherine, cortisol	ANS (sympathetic nervous system)
Reproduction	Gonads (ovaries, testes)	Androgens (testosterone), estrogens, progestins (progesterone)	ANS (parasympathetic nervous system)
Osmoregulation	Adrenal Glands Kidneys Liver	Aldosterone ADH Angiotensin	ANS (sympathetic and parasympathetic nervous system)

Homeostatic Imbalance: Endocrine System Disorders

Diseases of the endocrine system are common, and include diseases such as diabetes, thyroid disease, and obesity. An endocrine disease is usually characterized by hyposecretion or hypersecretion of hormones and an inappropriate response to hormone signaling by cells.

Cancer can occur in endocrine glands, such as the thyroid, and some hormones are involved in signaling distant cancer cells to multiply. For example, the estrogen receptor has been shown to be involved in certain types of breast cancers.

Hyposecretion

Hyposecretion is the production no hormone or too little of a hormone. It can be caused by the destruction of hormone-secreting cells, such as in Type 1 diabetes, or by a deficiency in a nutrient that is important for hormone synthesis. Hyposecretion can be treated with hormone-replacement therapies. Type 1 diabetes is an autoimmune disease that results in the destruction of the insulin-producing beta cells of the pancreas. A person with Type 1 diabetes needs insulin replacement therapy, usually by injection or insulin pump, in order to stay alive. An insulin pump is shown in **Figure** 1.54.

Diabetes insipidus is characterized by excretion of large amounts of very dilute urine, even if liquid intake

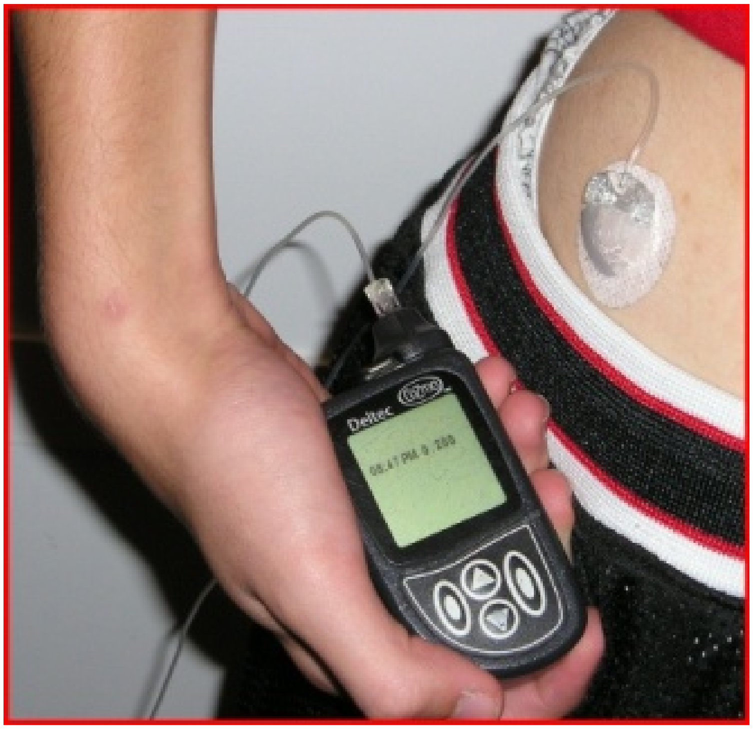

Figure 1.54: In the treatment of Type 1 diabetes, an insulin pump is an alternative to multiple daily injections of insulin. The pump is usually used along with the monitoring of blood glucose concentration and carbohydrate intake.

is reduced. It is caused by an inability of the kidney to concentrate urine due to a lack of antidiuretic hormone (ADH) also called vasopressin, or by an insensitivity of the kidneys to that hormone. Blood glucose levels are not affected in diabetes insipidus.

Growth hormone deficiency is caused by a lack of GH production by the pituitary. GH deficiency affects bone growth development, and people with growth hormone deficiency tend to have, among other things, low bone density and small stature, a condition called pituitary dwarfism. GH deficiency is treated by growth hormone replacement.

Hypothyroidism is the state in which not enough thyroid hormones are made. Thyroiditis is an autoimmune disease where the body's own antibodies attack the cells of the thyroid and destroy it. Thyroid hormones play an important role in brain development during fetal growth. Cells of the brain are a major target for the T3 and T4 hormones. As a result, hypothyroidism in children, either due to a thyroid problem from birth or a lack of iodine in the diet, is a major cause of physical and mental growth impairment in developing countries. In fact, iodine deficiency disorders are the single most common cause of preventable mental retardation and brain damage in the world.

Hypersecretion

Hypersecretion of a hormone happens when the body produces too much of a hormone. A hormone can be hypersecreted if the gland develops a tumor and grows out of control, or if the gland is signaled to produce too much of a hormone.

Hyperthyroidism is the result of excess thyroid hormone production, which causes an overactive metabolism and increased speed of all the body's processes. Hyperthyroidism is the most common cause of goiter in

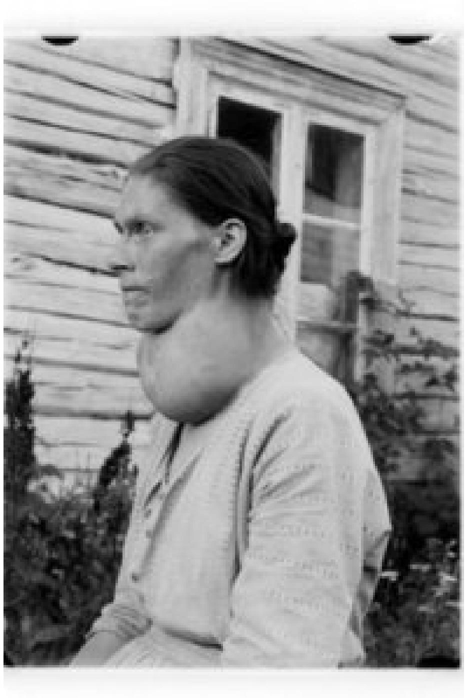

Figure 1.55: There are many causes of goiter, but the most common is the world is iodine deficiency. Today, iodine deficiency remains mostly a problem in poorer countries which lack the means to add iodine to foods. Iodized salt has helped reduce the amount of iodine deficiency in the developed world. Governments of some countries add iodine to cattle feed to ensure that dairy foods will contain iodine.

the developed world, shown in **Figure** 1.55.

Hypersecretion of growth hormone causes acromegaly. A common cause of acromegaly is a benign tumor of the pituitary glands that releases too much GH. In some cases, acromegaly is also caused by overproduction of the hypothalamus hormone growth hormone release hormone (GHRH). Acromegaly most commonly affects middle-aged adults and can result in serious illness and premature death. Symptoms include enlarged hands and feet, protruding brow and chin, and enlarged internal organs. However, the disease is hard to diagnose in the early stages and is frequently missed for many years due to its slow progression. If the pituitary produced too much GH during childhood, the person will be taller than normal, a condition called pituitary gigantism. Pituitary gigantism is very rare, and some of the tallest people on record had this condition.

Hormone Insensitivity: Type 2 Diabetes

In some cases, the body makes enough hormones, but body cells do not respond. This can be due to missing or defective hormone receptors, or the body cells become resistant to normal concentration of the hormone, and do not respond to it.

Type 2 diabetes is characterized by hyperglycemia (high blood glucose concentrations), body cells that do not respond to normal amounts of insulin (insulin resistance), and the resulting inability of the pancreas to produce enough insulin. Insulin resistance in cells results in high amounts of free fatty acids and glucose in the blood. High plasma levels of insulin and glucose due to insulin resistance often lead to metabolic syndrome and Type 2 diabetes. Type 2 diabetes can be controlled by improving the diet, increasing levels of activity, and sometimes medication.

Gestational diabetes is a form of diabetes that affects pregnant women. There is no known single cause, but it's believed that the hormones produced during pregnancy reduce the ability of the cells in the pregnant woman's body to respond to insulin, which results in high blood glucose concentrations.

Hormones as Medicines

Many hormones and molecules like them are used as medicines. The most common type of therapy is called **hormone-replacement therapy**. The most commonly-prescribed hormones are estrogens and synthetic progesterone (as methods of hormonal contraception and as HRT therapy for post-menopausal women), thyroxine (as levothyroxine, for hypothyroidism) and corticosteroids (for autoimmune diseases and several respiratory disorders). Progestin, a synthetic progesterone, is also used to prolong pregnancy in women who have experienced a miscarriage due to a premature drop in progesterone levels. Hydrocortisone is a synthetic form of cortisol that is used to treat allergies and inflammation as well as cortisol production deficiencies. Hydrocortisone cream is a common over-the-counter medication for the topical treatment of rash. Insulin is used by many people with diabetes.

Epinephrine

Because of its anti inflammatory effect on the immune system, epinephrine is used to treat anaphylaxis. Anaphylaxis is a sudden and severe allergic reaction that involves the entire body. After an initial exposure to a substance like a certain food (such as peanuts), or bee sting, a person's immune system can becomes sensitized to that substance, which is called an **allergen**. Upon second exposure, an allergic reaction occurs.

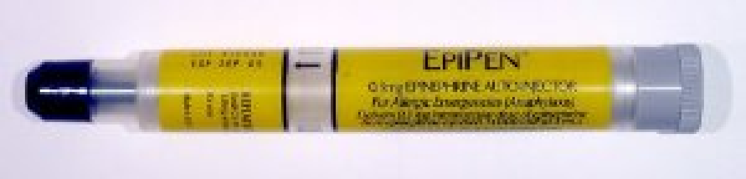

Figure 1.56: An EpiPen

Histamine and other substances that are released by body cells cause the blood vessels to dilate, which lowers blood pressure, and fluid to leak from the bloodstream into the tissues, which lowers the blood volume. The release of histamine causes the face and tongue to swell. Swelling of the lining of the throat can lead to breathing difficulties. The hormone epinephrine causes blood vessels to constrict which reduces swelling and causes blood pressure to increase. Epinephrine is used as a medicine in auto-injectors, shown in **Figure** 1.56, which a person can use themselves should they have an anaphylactic reaction.

Anabolic Androgenic Steroids

Synthetic androgens, in the form of anabolic androgenic steroids (anabolic steroids), have many medical uses. It is used to stimulate bone growth and appetite, induce puberty in boys, and treat muscle-wasting conditions in patients that have diseases such as cancer and AIDS. In general, androgens, including testosterone, promote protein synthesis and the growth of muscle tissue and other tissues that have androgen receptors. Androgens also block the effects of the stress hormone cortisol on muscle tissue, so the breakdown of muscle is greatly reduced.

Figure 1.57: Athletes involved in sports that emphasize strength, weight, and shape may feel pressure to take anabolic steroids, however, the majority of school athletes do not take them.

Anabolic Steroid Abuse

As a result of their muscle-building action, anabolic steroids are used in sport and bodybuilding to increase muscle size and strength, to gain a competitive edge or to assist in recovery from injury. Steroids used to gain competitive advantage are forbidden by the rules of the governing bodies of many sports. Serious health risks can be produced by long-term use or excessive doses of anabolic steroids. Most of these side effects are dose dependent, the most common being an increase in low density lipoprotein (bad cholesterol), and a decrease in good high density lipoprotein (good cholesterol). Anabolic steroids also increase the risk of cardiovascular disease in men with high risk of bad cholesterol. Acne is fairly common among anabolic steroid users, mostly due to increases in testosterone which stimulates the sebaceous glands to produce more oil. High doses of anabolic steroids have been linked to liver damage.

Teenagers, particularly boys, who take anabolic steroids, are more likely to be involved in sports that emphasize weight and shape, (such as football or wrestling, which is shown in **Figure** 1.57). Such teens also have higher rates of disordered eating, drug abuse, and generally have poorer attitudes towards health. Severe side effects can occur if a teenager uses anabolic steroids. For example, the steroids may prematurely stop the lengthening of bones, resulting in stunted growth. Other effects include, but are not limited to, accelerated bone maturation, increased acne outbreaks, and premature sexual development.

In addition to dangerous side effects of the steroids themselves, dangerous drug-taking habits that have been reported by abusers include: unsafe injection practices such as reusing needles, sharing needles, and sharing multidose vials. A common practice among anabolic steroid abusers is self–medicating with other hormones such as growth hormone and insulin, which in itself can lead to serious health consequences. Testosterone and other anabolic steroids are classified as a controlled substance in the United States (US), Canada, the United Kingdom (UK), Australia, Argentina, and Brazil.

Lesson Summary

- The endocrine system is a system of organs that release hormones into the blood. Unlike the nervous system whose action helps the body react immediately to change, the endocrine system controls changes that happen to the body over a long period of time.
- Hormones are made and secreted by cells in endocrine glands. The body produces many different

hormones, but each hormone is very specific for its target cells.

- The hypothalamus links the nervous system to the endocrine system by the pituitary gland. The pituitary gland secretes hormones that regulate homeostasis and also secretes hormones that stimulate other endocrine glands. Together the two glands serve as the major control centers of the endocrine system.
- The ovaries of females and the testes of males are the gamete producing organs, or gonads. In addition to producing gametes, an exocrine action, the gonads are endocrine glands that produce steroid sex hormones.
- The rate of hormone production and secretion is often regulated by homeostatic feedback control mechanisms, and the effect of hormones is controlled by hormone antagonists. In these ways, the concentration of hormones and their products is kept within a narrow range so as to maintain life.
- A feedback control mechanism, or a feedback loop, is a signaling system in which a product or effect of the system controls an earlier part of the system, either by shutting the process down or speeding it up.
- Diseases of the endocrine system are common, and include diseases such as diabetes, thyroid disease, and obesity. Many hormones and hormone-like molecules are used as medicines. The most common type of therapy is called hormone-replacement therapy.

Review Questions

1. How does a hormone initially activate a target cell?
2. What is the main difference between the locations of the receptors for amino acid-based hormones and steroid-based hormones?
3. List five main endocrine glands, and identify their locations.
4. Name the two glands that control the nervous system.
5. Name three hormones that are involved in the stress response and identify their function.
6. Outline the role of the parathyroid glands in regulation of blood calcium levels.
7. What hormone is secreted by the pineal gland, and what is the function of the hormone?
8. How do feedback mechanisms help maintain homeostasis?
9. How does negative feedback differ from positive feedback?
10. Identify an antagonistic pair of hormones and describe their action.
11. Why do you think the pituitary has two lobes?
12. What is the purpose of hormone replacement therapy?
13. Why might a problem with the pituitary gland affect many different parts of the body?
14. Your friend says that he's pretty sure that the adrenal medulla is controlled by hormones from the pituitary. Do you agree? Explain your answer.
15. Outline the feedback mechanism involved in glucose metabolism. Is this feedback mechanism positive or negative?
16. Positive feedback mechanisms are harmful to the body. Do you agree with this statement? Explain your answer.
17. Goiter is a swelling of the thyroid gland, which is commonly caused by a lack of iodine in the diet. Why do you think a lack of iodine causes the thyroid to swell?
18. Use the image of the feedback mechanisms to answer the two questions that follow.
19. Identify four hormones involved in these feedback mechanisms.

Further Reading / Supplemental Links

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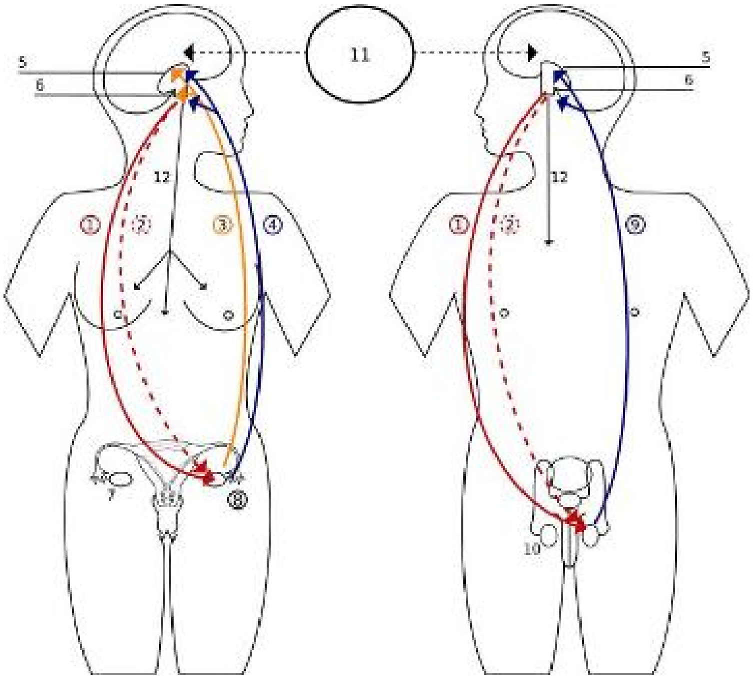

Figure 1.58: Identify three endocrine glands are involved in the feedback mechanisms shown in the figure.

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- Adapted from abstract: Anabolic Androgenic Steroids: A Survey of 500 Users Andrew B. Parkinson; Nick A. Evans (Medicine and Science in Sports and Exercise) at
- http://www.medscape.com/viewarticle/533461
- Adapted from:
- http://www.ncbi.nlm.nih.gov/sites/entrez?cmd=Retrieve&#38;amp;db=pubmed&#38;amp;dopt=AbstractPlu uids=11927236
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- http://web.indstate.edu/thcme/mwking/peptide-hormones.html#receptors
- http://web.indstate.edu/thcme/mwking/steroid-hormones.html
- http://www.ncbi.nlm.nih.gov/sites/entrez?cmd=Retrieve&#38;amp;db=pubmed&#38;amp;dopt=AbstractPlu uids=15589268
- http://www.nlm.nih.gov/medlineplus/ency/article/000844.htm#Definition
- http://www.hormone.org/
- http://www.hormone.org/
- http://www.nlm.nih.gov/medlineplus/endocrinesystem
- http://health.nih.gov/search.asp/24
- http://www.askabiologist.org.uk/
- http://en.wikipedia.org

Vocabulary

amino acid-based hormones Hormones made of amino acids; not fat-soluble and therefore cannot diffuse through the plasma membrane of their target cell; usually bind to receptors that are found on the cell membrane.

antagonistic Hormones that have opposite actions on the body, such as insulin and glucagons.

cholesterol-based hormones Hormones made of lipids such as phospholipids and cholesterol; also called steroid hormones; are fat soluble and are able to diffuse through the plasma membrane; bind to receptors that are found within the cell cytosol and nucleus.

circadian rhythm A roughly-24-hour cycle in the biological processes carried out within organisms, including plants, animals, fungi and certain bacteria.

cortisol A steroid hormone produced by the adrenal glands; often called the ”stress hormone” as it is involved in the body’s response to stress; increases blood pressure, blood sugar levels and has an immunosuppressive action.

direct gene activation A system in which a fat-soluble hormone diffuses across the membrane and binds to the receptor within the cytosol or nucleus. The hormone-receptor complex then acts as a transcription factor that affects gene expression.

endocrine glands Ductless organs that make and secrete hormones directly into the blood or the fluid surrounding a cell rather than through a duct.

endocrine system A system of organs that releases chemical message molecules, called hormones, into the blood.

exocrine glands Organs that secrete their products into ducts (they are duct glands); do not secrete hormones; secrete products such as water, mucus, enzymes, and other proteins through ducts to specific locations inside and outside the body.

feedback control mechanism A signaling system in which a product or effect of the system controls an earlier part of the system, either by shutting the process down or speeding it up; also known as a feedback loop.

glucagon An important hormone involved in carbohydrate metabolism; released when the glucose level in the blood is low which causes the liver to change stored glycogen into glucose and release it into the bloodstream.

gonads The gamete producing organs; the ovaries of females and the testes of males.

hormone-like substances Refers to a group of signaling molecules that are derived from certain types of fatty acids and proteins.

hormones Chemical messenger molecules that are made by cells in one part of the body and cause changes in cells in another part of the body.

hypersecretion The production of too much of a hormone.

hyposecretion The production of no hormone or too little of a hormone.

hypothalamus Area of the brain that coordinates many seasonal and circadian rhythms, complex homeostatic mechanisms, and the autonomic nervous system (ANS).

islets of Langerhans Areas of the pancreas with groupings of endocrine cells; produce the amino acid-based hormones insulin, glucagon, and somatostatin.

negative feedback A reaction in which the system responds in such a way as to reverse the direction of change.

neuropeptides Hormone-like substance; signaling peptides found in nervous tissue.

positive feedback A reaction in which the system responds in such a way as to speed up the direction of change.

prostaglandins Hormone-like substance made from essential fatty acids; produced by most cells in the body; have many different effects such as causing constriction or dilation of blood vessels but they are all are localized within the target cells and tissues.

puberty The process of physical changes during which the sex organs mature and a person become capable of reproducing.

second messenger system A system in which a water-soluble hormone molecule does not enter the cell, instead it binds to the membrane-bound receptor molecule, which triggers changes within the cell. These changes are activated by second messenger molecules.

sex hormones Hormones that are responsible for the secondary sex characteristics that develop at puberty.

signal transduction pathway Process initiated by the binding of a hormone to its receptor; a process of molecular changes that turns the hormone's extracellular signal into an intracellular response.

target cell The cell on which a hormone has an effect; has receptor proteins that are specific to the hormone.

Points to Consider

- Think about some of the problems people may have to their muscular systems if their nervous system is not functioning correctly.
- Propose what would happen if the hypothalamus did not produce ADH.
- Why are negative feedback loops more common than positive feedback loops?

Chapter 2

Muscular, and Integumentary(sk in) Systems

2.1 Muscular System (as it relates to the nervous system)

Lesson Objectives

- Explain how muscle fibers contract.
- Examine the role of ATP and calcium in muscle contraction.
- Explain how muscles respond to aerobic and anaerobic exercise.

Introduction

The muscular system is the biological system of humans that allows them to move. The muscular system, in vertebrates, is controlled through the nervous system. Much of your muscle movement occurs without your conscious control and is necessary for your survival. The contraction of your heart and peristalsis, the intestinal movements that pushes food through your digestive system, are examples of involuntary muscle movements. Involuntary muscle movement is controlled by the autonomic nervous system. Voluntary muscle contraction is used to move the body and can be finely controlled, such as the pincer-type movement of the fingers that is needed to pick up chess pieces, or the gross movements of legs arm, and the torso that are needed in skating, shown in **Figure** 2.1. Voluntary muscle movement is controlled by the somatic nervous system.

Muscle Tissues

Each muscle in the body is composed of specialized structures called muscle fibers. **Muscle fibers** are long, thin cells that have a special talent that other cells do not have—they are able to contract. Muscles, where attached to bones or internal organs and blood vessels, are responsible for movement. Nearly all movement in the body is the result of muscle contraction. Exceptions to this are the action of cilia, the flagellum on sperm cells, and the amoeboid movement of some white blood cells.

Three types of muscle tissue are in the body: skeletal, smooth, and cardiac.

Figure 2.1: You need muscles to play chess. Playing chess requires fine motor movement, but not a lot of gross muscle movements. Skating on the other hand, requires a lot of gross muscle movement of the limbs and the entire body.

- **Skeletal muscle** is usually attached to the skeleton. Skeletal muscles are used to move the body. They generally contract voluntarily (controlled by the somatic nervous system), although they can also contract involuntarily through reflexes.
- **Smooth muscle** is found within the walls of organs and structures such as the esophagus, stomach, intestines, bronchi, uterus, urethra, bladder, and blood vessels. Unlike skeletal muscle, smooth muscle is involuntary muscle which means it not under your conscious control.
- **Cardiac muscle** is also an involuntary muscle but is a specialized kind of muscle found only within the heart.

Cardiac and skeletal muscles are striated, in that they contain highly-regular arrangements of bundles of protein fibers that give them a “striped” appearance. Smooth muscle does not have such bundles of fibers, and is non-striated. While skeletal muscles are arranged in regular, parallel bundles, cardiac muscle fibers connect at branching, irregular angles. Skeletal muscle contracts and relaxes in short, intense bursts, whereas cardiac muscle contracts constantly for 70 to 80 years (an average life span), or even longer.

Skeletal Muscle

Skeletal muscle, which is attached to bone, is responsible for body movements and body posture. There are approximately 639 skeletal muscles in the human body, some of which are shown in **Figure** 2.2. These muscles are under conscious, or voluntary, control. The basic units of skeletal muscle are muscle cells that have many nuclei. These muscle cells also contain light and dark stripes called striations, which are shown in **Figure** 2.3. The striations are a result of the orientation of the contractile proteins inside the cells. Skeletal muscle is therefore called striated muscle. Each muscle cell acts independently of its neighboring muscle cells. On average, adult males are made up of 40 to 50 percent skeletal muscle tissue and an adult female is made up of 30 to 40 percent skeletal muscle tissue.

Smooth Muscle

Smooth muscle is found in the walls of the hollow internal organs such as blood vessels, the intestinal tract, urinary bladder, and uterus. It is under control of the autonomic nervous system. This means that smooth muscle cannot be controlled consciously, so it is also called involuntarily muscle. Smooth muscle cells do not have striations, and so smooth muscle is also called non-striated muscle. Smooth muscle cells are spindle-shaped and have one central nucleus. The cells are generally arranged in sheets or bundles, rather than the regular grouping that skeletal muscle cells form, and they are connected by gap junctions. Gap junctions are little pores or gaps in the cell membrane that link adjoining cells and they allowing

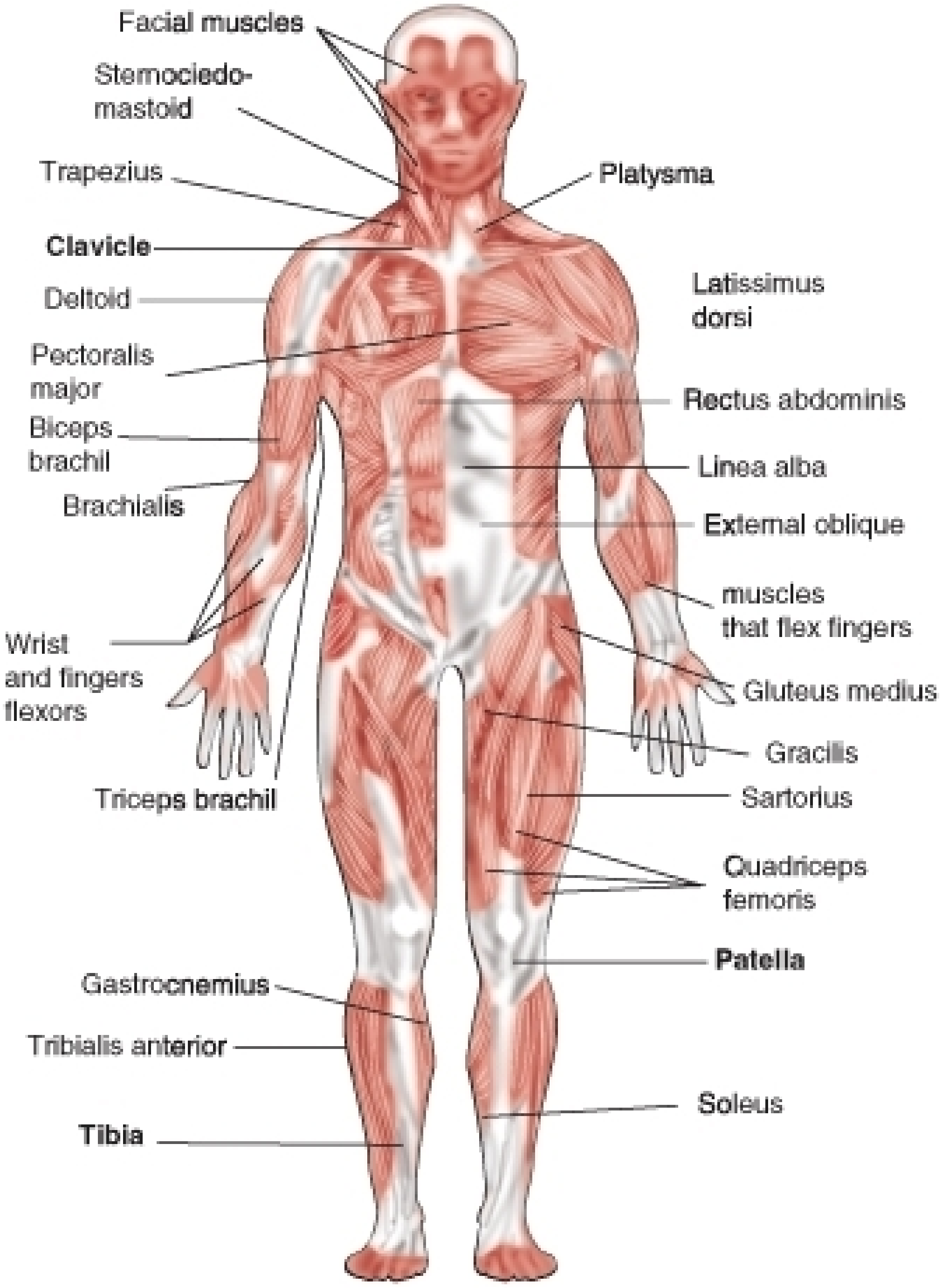

Figure 2.2: Frontal view of the major skeletal muscles. You would not see smooth and cardiac muscles included in diagrams of the muscular system because such diagrams usually show only the muscles that move the body (skeletal muscles).

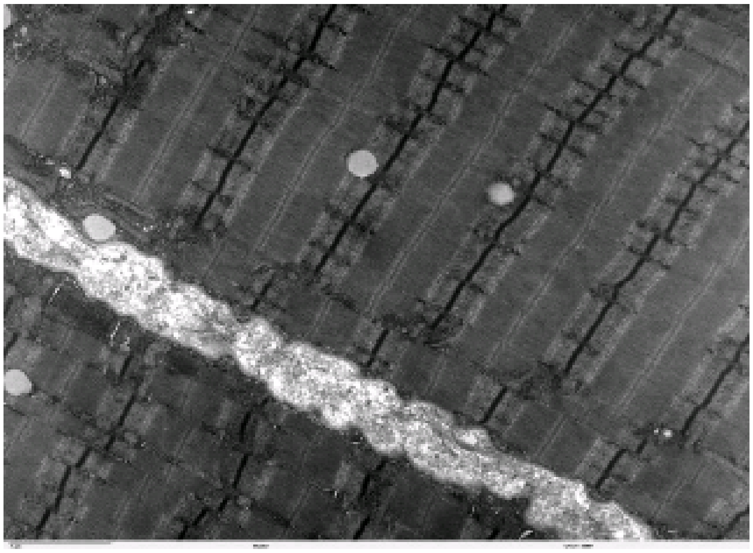

Figure 2.3: Micrograph of skeletal muscle. The stripy appearance of skeletal muscle tissue is due to long protein filaments that run the length of the fibers.

quick passage of chemical messages between cells. Smooth muscle is very different from skeletal muscle and cardiac muscle in terms of structure and function, as shown in **Figure** 2.4. Smooth muscle contracts slowly and rhythmically.

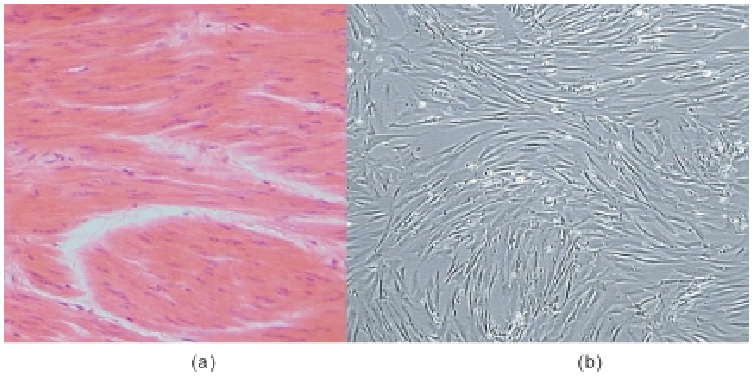

Figure 2.4: Smooth muscle. The appearance of smooth muscle is very different from skeletal and cardiac muscle. The muscle protein fibers within smooth muscle are arranged very differently to the protein fibers of skeletal or cardiac fibers, shown in (a). The spindly shape of smooth muscle cells can be seen in (b).

Cardiac Muscle

Cardiac muscle, which is found in the walls of the heart, is under control of the autonomic nervous system, and so it is an involuntary muscle. A cardiac muscle cell has characteristics of both a smooth muscle and skeletal muscle cell. It has one central nucleus, similar to smooth muscle, but it striated, similar to skeletal muscle. The cardiac muscle cell is rectangular in shape, as can been seen in **Figure** 2.5. The contraction of cardiac muscle is involuntary, strong, and rhythmical. Cardiac muscle has many adaptations that makes it highly resistant to fatigue. For example, it has the largest number of mitochondria per cell of any muscle type. The mitochondria supply the cardiac cells with energy for constant movement. Cardiac cells also contain myoglobins (oxygen-storing pigments), and are provided with a large amount of nutrients and oxygen by a rich blood supply.

Cardiac muscle is similar to skeletal muscle in chemical composition and action. However, the structure of cardiac muscle is different in that the muscle fibers are typically branched like a tree branch, and connect to other cardiac muscle fibers through intercalcated discs, which are a type of gap junction. A close-up of an intercalated disc is shown in **Figure** 2.5. Cardiac muscle fibers have only one nucleus.

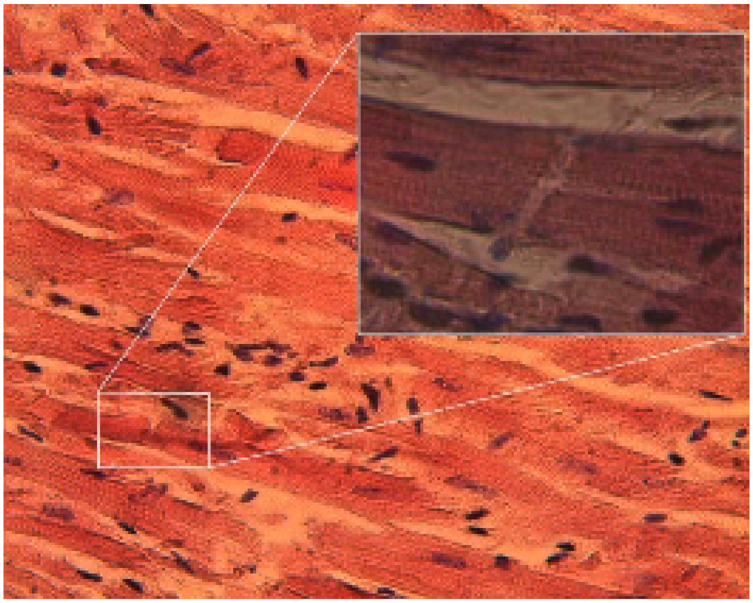

Figure 2.5: Cardiac muscle. Cardiac muscle fibers are connected together through intercalated discs.

Structure of Muscle Tissue

A whole skeletal muscle is an organ of the muscular system. Each skeletal muscle consists of skeletal muscle tissue, connective tissue, nerve tissue, and vascular tissue. Skeletal muscles vary considerably in size, shape, and arrangement of fibers. They range from extremely tiny strands such as the tiny muscles of the middle ear to large masses such as the quadriceps muscles of the thigh.

Each skeletal muscle fiber is a single large, cylindrical muscle cell. Skeletal muscle fibers differ from "regular" body cells. They are multinucleated, which means they have many nuclei in a single cell; during development many stem cells called myoblasts fuse together to form muscle fibers. Each nucleus in a fiber originated from a single myoblast. Smooth and cardiac muscle fibers do not develop in this way.

An individual skeletal muscle may be made up of hundreds, or even thousands, of muscle fibers that are bundled together and wrapped in a connective tissue covering called epimysium. Fascia, connective tissue outside the epimysium, surrounds and separates the skeletal muscles. Portions of the epimysium fold inward to divide the muscle into compartments called fascicles. Each fascicle compartment contains a bundle of muscle fibers, as shown in **Figure** 2.6.

Skeletal muscle fibers, like body cells, are soft and fragile. The connective tissue covering give support and protection for the delicate cells and allow them to withstand the forces of contraction. The coverings also provide pathways for the passage of blood vessels and nerves. Active skeletal muscle needs efficient delivery of nutrients and oxygen, and removal of waste products, both of which are carried out by a rich supply of blood vessels.

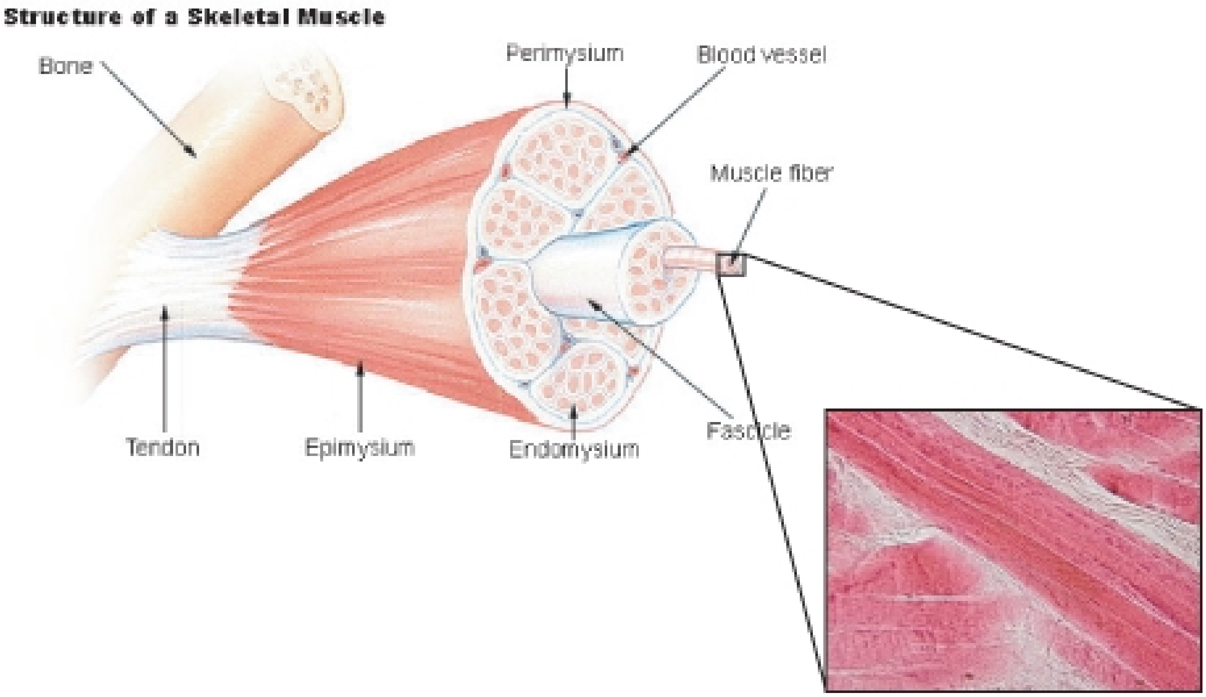

Figure 2.6: Individual bundles of muscle fibers are called fascicles. The cell membrane surrounding each muscle fiber is called the

Muscles and Bones

Muscles move the body by contracting against the skeleton. Muscles can only actively contract, they extend (or relax) passively. The ability of muscles to move parts of the body in opposite directions requires that they be attached to bones in pairs which work against each other (called antagonistic pairs). Generally, muscles are attached to one end of a bone, span a joint, and are attached to a point on the other bone of the joint. Commonly, the connective tissue that covers the muscle extends beyond the muscle to form a thick ropelike structure called a tendon, as shown in **Figure** 2.6. One attachment of the muscle, the origin, is on a bone that does not move when the muscle contracts. The other attachment point, the insertion, is on the bone that moves. Tendons and muscles work together and exert only a pulling force on joints.

For example, when you contract your biceps brachii muscles, shown in **Figure** 2.7, the force from the muscles pulls on the radius bone (its point of insertion) causing the arm to move up. This action decreases the angle at the elbow joint (flexion). Flexion of the elbow joint is shown in **Figure B** 2.8. A muscle that causes the angle of a joint to become smaller is called a **flexor**. To extend, or straighten the arm, the biceps brachii relaxes and the triceps on the opposite side of the elbow joint contracts. This action is called extension, and a muscle that causes a joint to straighten out is called an **extensor**. In this way the joints of your body act like levers that reduce the amount of effort you have to expend to cause large movements of the body.

Muscle Contraction

A **muscle contraction** occurs when a muscle fiber generates tension through the movement of actin and myosin. Although you might think the term contraction means only ”shortening,” the overall length of a contracted muscle may stay the same, or increase, depending on the force working against the muscle.

Each muscle fiber contains cellular proteins and hundreds or thousands of myofibrils. Each **myofibril** is a

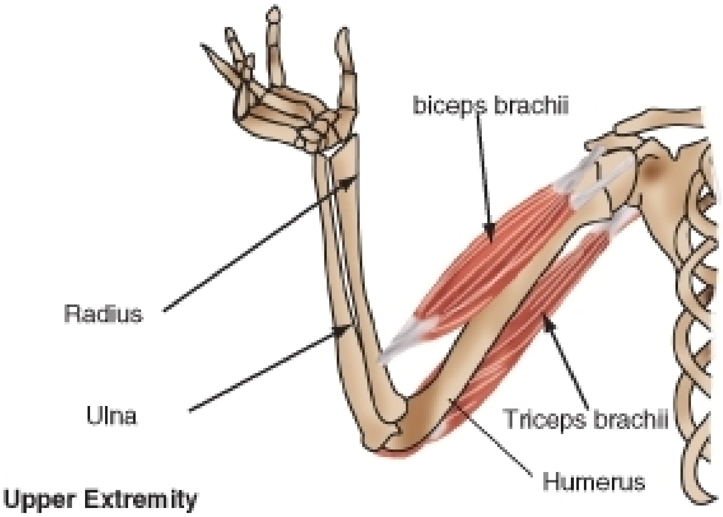

Figure 2.7: Movement of the elbow joint involves muscles and bones. The contraction of the biceps brachii muscle pulls on the radius, its point of insertion, which causes the arm to bend. To straighten the arm, the triceps brachii muscle contracts and pulls on the ulna, this causes the arm to straighten.

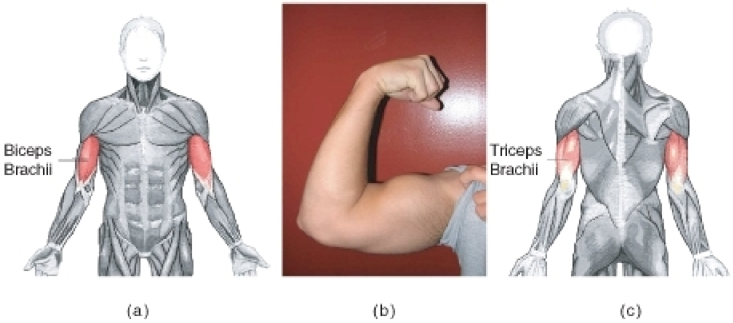

Figure 2.8: (a) The position of the biceps brachii. (b) The biceps brachii and triceps brachii act as an atagonistic pair of muscles that move the arm at the elbow joint. The biceps muscle is the flexor, and the triceps, at the back of the arm, is the extensor (c).

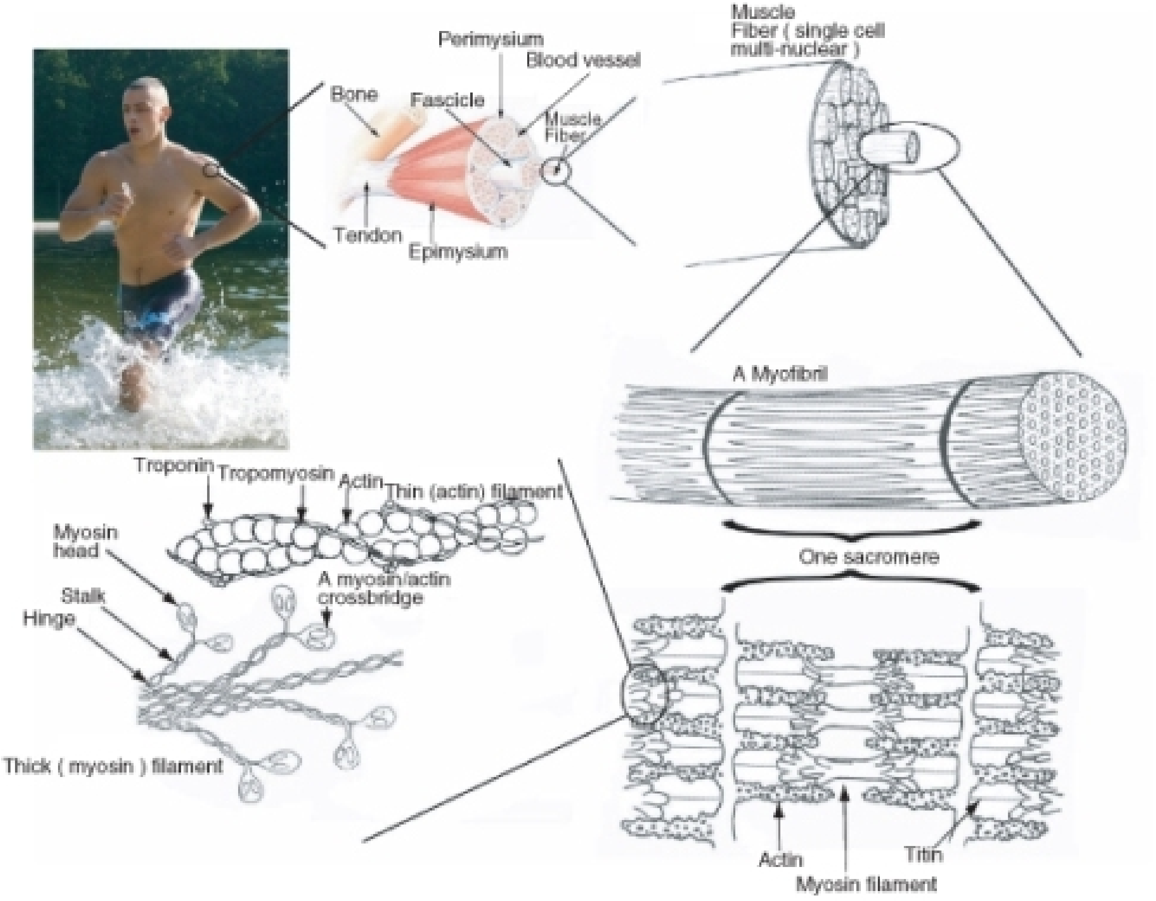

Figure 2.9: The components of muscle contraction. The sacromere is the functional unit of muscle contraction; it reaches from one Z-line to the next (also shown in

long, cylindrical organelle that is made up of two types of protein filaments: actin and myosin. The **actin** filament is thin and threadlike, the **myosin** filament is thicker. Myosin has a "head" region that uses energy from ATP to "walk" along the actin thin filament (**Figure** 2.13). The overlapping arrangement of actin and myosin filaments gives skeletal muscle its striated appearance. The actin and myosin filaments are organized into repeating units called **sarcomeres,** which can be seen in **Figure** 2.9. The thin actin filaments are anchored to structures called Z lines. The region from one Z line to the next makes up one sacromere. When each end of the myosin thick filament moves along the actin filament, the two actin filaments at opposite sides of the sacromere are drawn closer together and the sarcomere shortens, as shown in **Figure** 2.10. When a muscle fiber contracts, all sarcomeres contract at the same time, which pulls on the fiber ends.

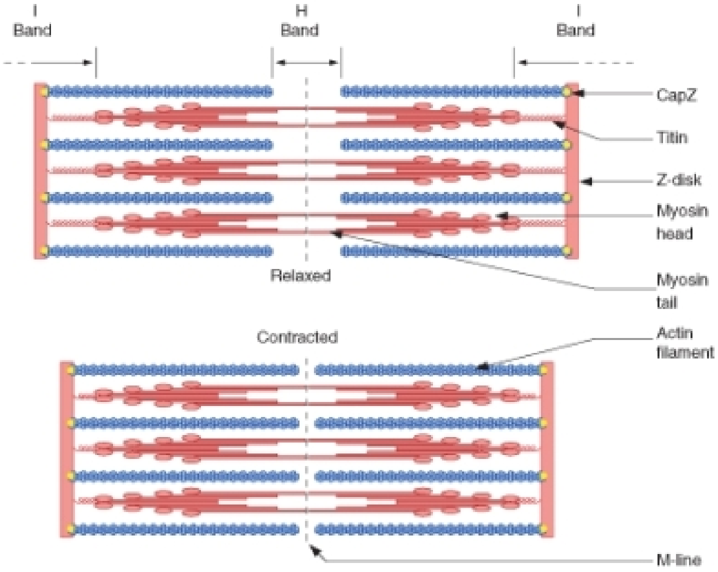

Figure 2.10: When each end of the myosin thick filament moves along the actin filament, the two actin filaments at opposite sides of the sacromere are drawn closer together and the sarcomere shortens.

The Neuromuscular Junction

For skeletal (voluntary) muscles, contraction occurs as a result of conscious effort that comes from the brain. The brain sends nerve signals, in the form of action potentials to the motor neuron that innervates the muscle fiber, such as the motor neuron in **Figure** 2.11. In the case of some reflexes, the signal to contract can originate in the spinal cord through a reflex arc. Involuntary muscles such as the heart or smooth muscles in the gut and vascular system contract as a result of non-conscious brain activity or stimuli endogenous to the muscle itself. Other actions such as body motion, breathing, and chewing have a reflex aspect to them; the contractions can be initiated consciously or unconsciously, but are continued through unconscious reflexes. You can learn more about action potentials and reflex arcs in the *Nervous and Endocrine Systems* chapter.

The Sliding Filament Theory

The widely accepted theory of how muscles contract is called the sliding-filament model (also known as the sliding filament theory), which is shown in **Figure** 2.12. The presence of calcium ions (Ca^{2+}) allows for the interaction of actin and myosin. In the resting state, these proteins are prevented from coming into contact.

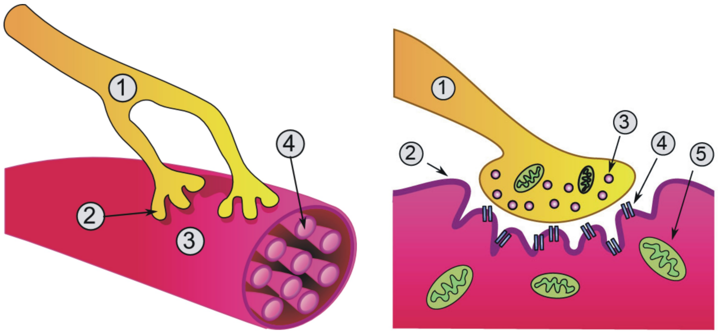

Figure 2.11: (a) A simplified diagram of the relationship between a skeletal muscle fiber and a motor neuron at a neuromuscular junction. 1. Axon; 2. Synaptical junction; 3. Muscle fiber; 4. Myofibril. (b) A close-up view of a neuromuscular junction. The neurotransmitter acetylcholine is released into the synapse and binds to receptors on the muscle cell membrane. The acetylcholine is then broken down by enzymes in the synapse. 1. presynaptic terminal; 2. sarcolemma; 3. synaptic vesicles; 4. Acetylcholine receptors; 5. mitochondrion. For an animation of the neuromuscular junction see

Two other proteins, troponin and tropomyosin, act as a barrier between the actin and myosin, preventing contact between them. When Ca^{2+} binds to the actin filament, the shape of the troponin-tropomyosin complex changes, allowing actin and myosin to come into contact with each other. Below is an outline of the sliding filament theory.

1. An action potential (see the *Nervous and Endocrine Systems* chapter) arrives at the axon terminal of a motor neuron.
2. The arrival of the action potential activates voltage-dependent calcium channels at the axon terminal, and calcium rushes into the neuron.
3. Calcium causes vesicles containing the neurotransmitter acetylcholine to fuse with the plasma membrane, which releases acetylcholine into the synaptic cleft between the axon terminal and the motor end plate of the skeletal muscle fiber.
4. Activation of the acetylcholine receptors on the muscle fiber membrane opens its sodium/potassium channel, which triggers an action potential in the muscle fiber.
5. The action potential spreads through the muscle fiber's network, depolarizing the inner portion of the muscle fiber.
6. The depolarization activates specialized storage sites throughout the muscle, called the sarcoplasmic reticulum, to release calcium ions (Ca^{++}). The sarcoplasmic reticulum is a special type of smooth endoplasmic reticulum found in smooth and skeletal muscle that contains large amounts of Ca^{++}, which it stores and then releases when the cell is depolarized.
7. The calcium ions bind to actin filaments of the myofibrils and activate the actin for attachment by the myosin heads filaments.
8. Activated myosin binds strongly to the actin filament. Upon strong binding, myosin rotates at the myosin-actin interface which bends a region in the "neck" of the myosin "head," as shown in **Figure 10**.
9. Shortening of the muscle fiber occurs when the bending neck of the myosin region pulls the actin and myosin filaments across each other. Meanwhile, the myosin heads remain attached to the actin filament, as shown in **Figure** 2.12.
10. The binding of adenosine triphosphate (ATP) allows the myosin heads to detach from actin. While detached, ATP breaks down to adenosine diphosphate and an inorganic phosphate (ADP + Pi). The breaking of the chemical bond in ATP gives energy to the myosin head, allowing it to bind to actin

again.

11. Steps 9 and 10 repeat as long as ATP is available and Ca^{++} is present on the actin filament. The collective bending of numerous myosin heads (all in the same direction) moves the actin filament relative to the myosin filament which causes a shortening of the sacromere. Overall, this process results in muscle contraction. The sarcoplasmic reticulum actively pumps Ca^{++} back into itself. Muscle contraction stops when Ca^{++} is removed from the immediate environment of the myofilaments.

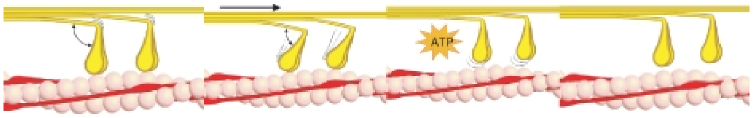

Figure 2.12: The process of actin and myosin sliding past one another is called crossbridge cycling, and it occurs in all muscle types. Myosin is a molecular motor that moves along the passive actin. Each thick myosin filament has little extensions or

Animation of a sarcomere shortening: http://highered.mcgraw-hill.com/sites/0072437316/student_view0/chapter42/a

Animation of Actin and Myosin bridging: (requires Quicktime) http://www.sci.sdsu.edu/movies/actin_myosin.html

Motor Units

It is important to remember that the sliding filament theory applies to groups of individual muscle fibers which, along with their motor neuron, are called **motor units**. A single, momentary contraction is called a muscle twitch. A twitch is the response to a single stimulus that can involve a number of motor units. As a stimulus increases, more motor units are stimulated to contract until a maximum level is reached at which point the muscle cannot exert any more force.

Each muscle fiber contracts on an ”all or nothing” principle, a muscle fiber either contracts fully, or not at all, and all the fibers in a single motor unit contract at the same time. When a muscle is required to contract during exercise not all motor units are contracted at the same time. Most movements require only a small amount of the total force possible by the contraction of an entire muscle. As a result, our nervous system grades the intensity of muscle contraction by using different numbers of motor units at a time.

Cardiac Muscle Contractions

Cardiac muscle is adapted to be highly resistant to fatigue: it has a large number of mitochondria which allow continuous aerobic respiration; numerous myoglobins (oxygen storing pigment); and a good blood supply, which provides nutrients and oxygen. The heart is so tuned to aerobic metabolism that it is unable to pump well when there is a lack of blood to the heart muscle tissue, which can lead to a heart attack.

Unlike skeletal muscle, which contracts in response to nerve stimulation, and like certain types of smooth muscle, cardiac muscle is able to initiate contraction by itself. As a result, the heart can still beat properly even if its connections to the central nervous system are completely severed. A single cardiac muscle cell, if left without input, will contract rhythmically at a steady rate; if two cardiac muscle cells are in contact, whichever one contracts first will stimulate the other to contract, and so on. This inherent ability to contract is controlled by the autonomic nervous system.

If the rhythm of cardiac muscle contractions is disrupted for any reason (for example, in a heart attack or a cardiac arrest), erratic contractions called fibrillation can result. Fibrillation, which is life threatening, can be stopped by use of a device called a defibrillator. Defibrillation consists of delivering a therapeutic dose of electrical energy to the heart which depolarizes part of the heart muscle. The depolarization stops the fibrillation, and allows a normal heartbeat to start up again. Most types of defibrillators are operated by medical personnel only. However, you may be familiar with an automated external defibrillator (AED) which is shown in **Figure** 2.13.

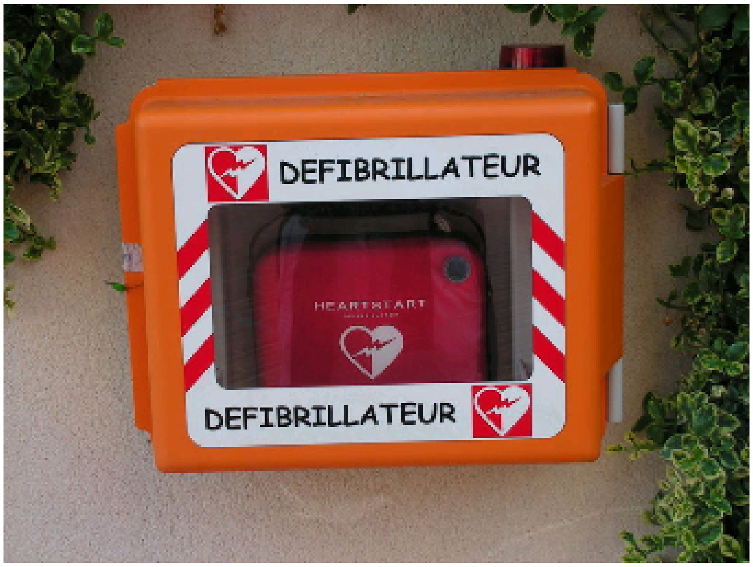

Figure 2.13: A wall-mounted automated external defibrillator (AED). Defibrillators are used to

Smooth Muscle Contraction

Smooth muscle-containing tissue, such as the stomach or urinary bladder often must be stretched, so elasticity is an important characteristic of smooth muscle. Smooth muscle (like cardiac muscle) does not depend on motor neurons to be stimulated. However, motor neurons of the autonomic nervous system do reach smooth muscle, causing it to contract or relax, depending on the type of neurotransmitter that is released. Smooth muscle is also affected by hormones. For example, the hormone oxytocin causes contraction of the uterus during childbirth.

Similar to the other muscle types, smooth muscle contraction is caused by the sliding of myosin and actin filaments over each other. However, calcium initiates contractions in a different way in smooth muscle than in skeletal muscle. Smooth muscle may contract phasically with rapid contraction and relaxation, or tonically with slow and sustained contraction. The reproductive, digestive, respiratory, and urinary tracts, skin, eye, and vasculature all contain smooth muscle. For example, the ability of vascular smooth muscle (veins and arteries) to contract and dilate is critical to the regulation of blood pressure. Smooth muscle contracts slowly and may maintain the contraction (tonically) for prolonged periods in blood vessels, bronchioles, and some sphincters. In the digestive tract, smooth muscle contracts in a rhythmic peristaltic fashion. It rhythmically massages products through the digestive tract, shown in **Figure** 2.14, as the result of phasic contraction.

Energy Supply for Muscle Contraction

Energy for the release and movement of the myosin head along the actin filament comes from ATP. The role of ATP in muscle contraction can be observed in the action of muscles after death, at which point

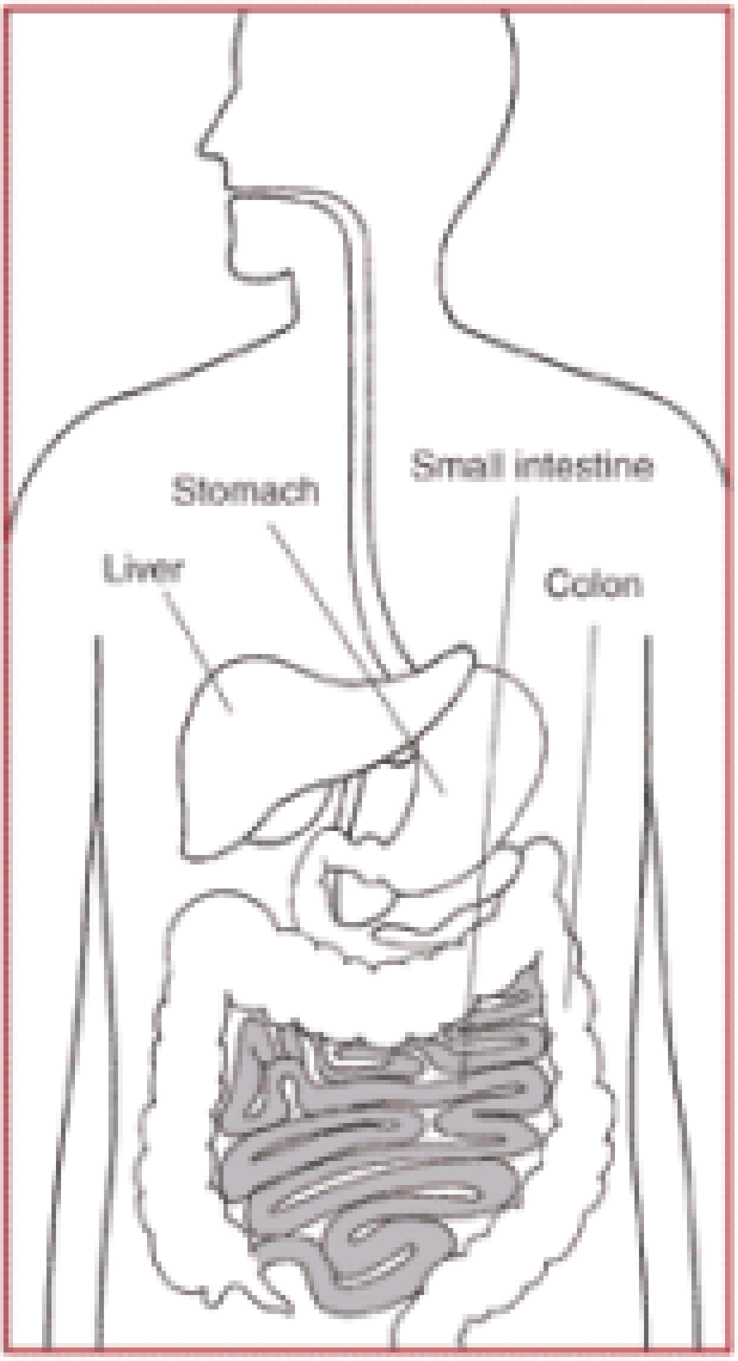

Figure 2.14: The intestinal tract contains smooth muscle which moves food along by contracting and relaxing in a process called peristalsis. An animation of peristalsis can be viewed at

ATP production stops. Without ATP, myosin heads are unable to release from the actin filaments, and remain tightly bound to it (a protein complex called actomyosin). As a result, all the muscles in the body become rigid and are unable to move, a state known as rigor mortis. Eventually, enzymes stored in cells are released, and break down the actomyosin complex and the muscles become ”soft” again.

Cellular respiration is the process by which cells make ATP by breaking down organic compounds from food. Muscle cells are able to produce ATP with oxygen which is called aerobic respiration, or without oxygen, an anaerobic process called anaerobic glycolysis or fermentation. The process in which ATP is made is dependent on the availability of oxygen (see *Cellular Respiration* chapter).

Aerobic ATP Production

During everyday activities and light exercise, the mitochondria of muscle fibers produce ATP in a process called aerobic respiration. **Aerobic respiration** requires the presence of oxygen to break down food energy (usually glucose and fat) to generate ATP for muscle contraction. Aerobic respiration produces large amounts of ATP, and is an efficient means of making ATP. Up to 38 ATP molecules can be made for every glucose molecule that is broken down. It is the preferred method of ATP production by body cells. Aerobic respiration requires large amount of oxygen, and can be carried out over long periods of time. As activity levels increase, breathing rate increases to supply more oxygen for increased ATP production.

Anaerobic ATP Production

When muscles are contracting very quickly, which happens during vigorous exercise, oxygen cannot travel to the muscle cells fast enough to keep up with the muscles’ need for ATP. At this point, muscle fibers can switch to a breakdown process that does not require oxygen. The process, called **anaerobic gylcolysis** (sometimes called anaerobic respiration) breaks down energy stores in the absence of oxygen to produce ATP.

Anaerobic glycolysis produces only two molecules of ATP for every molecule of glucose, so it a less efficient process than aerobic metabolism. However, anaerobic glycolysis produces ATP about 2.5 times faster than aerobic respiration does. When large amounts of ATP are needed for short periods of vigorous activity, glycolysis can provide most of the ATP that is needed. Anaerobic glycolysis also uses up a large amount of glucose to make relatively small amounts of ATP. In addition to ATP, large amounts of lactic acid are also produced by glycolysis. When lactic acid builds up faster than it can be removed from the muscle, it can lead to muscle fatigue. Anaerobic glycolysis can be carried out for only about 30 to 60 seconds. Some recent studies have found evidence that mitochondria inside the muscle fibers are able to break down lactic acid (or lactate) to produce ATP, and that endurance training results in more lactate being is taken up by mitochondria to produce ATP.

2.2 Integumentary System

Lesson Objectives

- Identify the structures that make up the integumentary system.
- Outline the role of the skin in providing a physical barrier to the external environment.
- Outline the structure of hair.
- Examine the structure of nails, and compare them to the structure of nails.

Introduction

Your **integumentary system** is the external covering of your body. It is made up of your skin, hair, and nails. The integumentary system of other animals such as birds and reptiles includes their feathers and scales. The name comes from the Latin term *integumentum*, which means "a covering."

Figure 2.15: Your skin acts like a waterproof barrier so that you can swim without water leaking into your body.

The integumentary system has multiple roles in homeostasis, including protection, temperature regulation, sensory reception, biochemical synthesis, and absorption. Keeping water out of the body is an important role for your integumentary system, as is shown by **Figure** 2.15. Your body systems all work together to maintain relatively stable internal conditions. Each of the parts that make up your integumentary system has a special role in maintaining homeostasis which we will explore a little later. An introduction to the Integumentary System can be viewed at http://www.youtube.com/watch?v=no_XRnoNGfE.

Structure and Function of Your Skin

The skin is a vital organ that covers the entire outside of the body, forming a protective barrier against pathogens and injuries from the environment. The skin is the body's largest organ, covering the entire outside of the body, and it is only about 2 mm thick. It shields the body against heat, light, injury, and infection. The skin also helps regulate body temperature, gathers sensory information from the environment, stores water, fat, and vitamin D, and acts as a physical barrier in protecting us from disease.

Your skin is constantly in contact with your external environment so it gets cut, scratched, and exposed to radiation, such as ultraviolet (UV) light. You also naturally shed many skin cells every day. Your body replaces damaged or missing skin cells by growing more of them, through the process of mitosis. Two distinct layers make up the skin: the epidermis and the dermis. A fatty layer, called subcutaneous tissue, or hypodermis (below skin), lies under the dermis, but it is not considered to be part of your skin. The layers that make up your skin are shown in **Figure** 2.16.

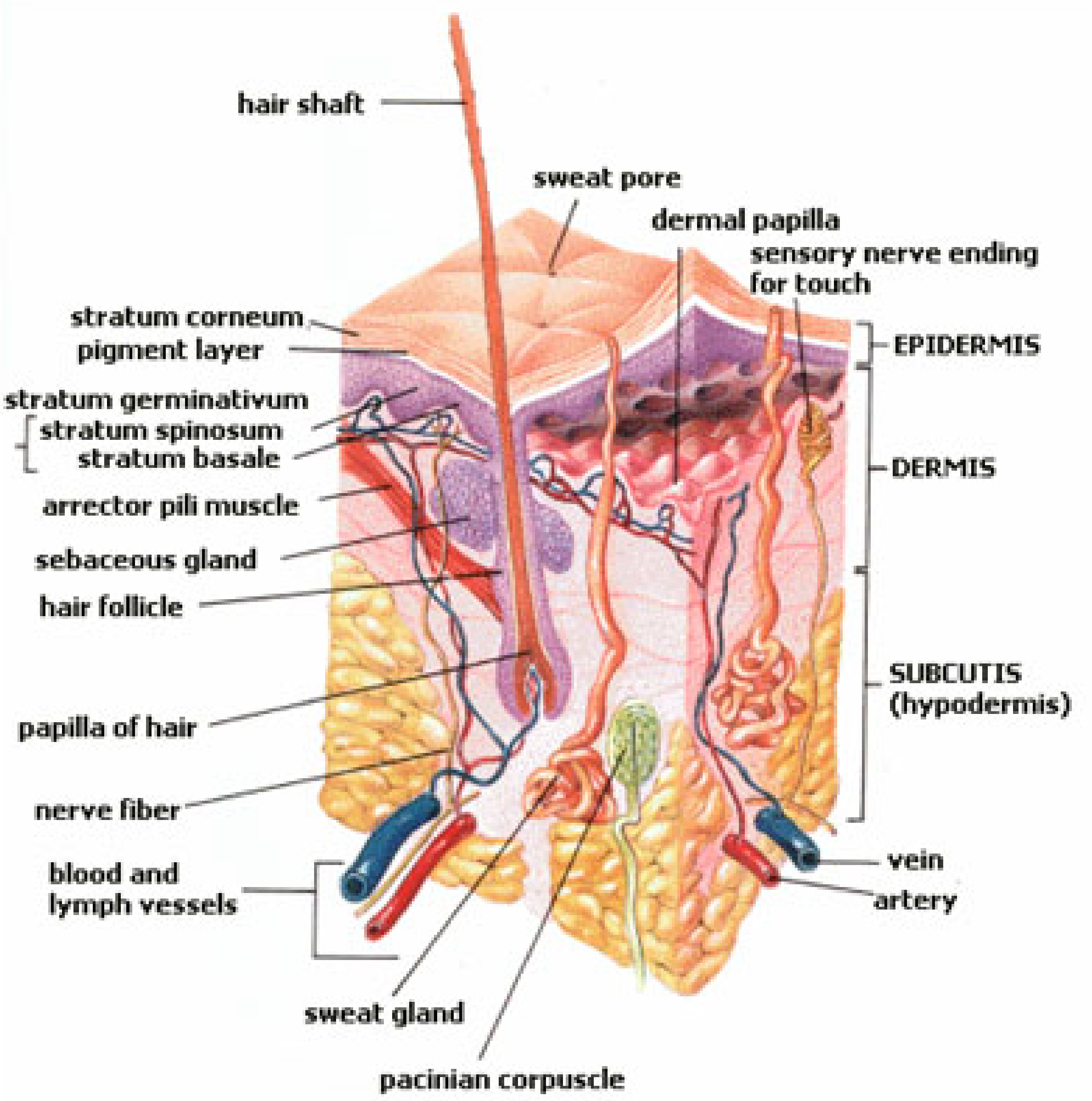

Figure 2.16: Structure of the skin. The structures of the epidermis, dermis, and the subcutaneous tissue (called the subcutis in this diagram). Note how there are no blood vessels in the epidermis.

The color, thickness and texture of skin vary over the body. There are two general types of skin; thin and hairy, which is the most common type on the body, and thick and hairless, which is found on parts of the body that are used heavily and experience a lot of friction, such as the palms of the hands or the soles of the feet.

Functions of Skin: Skin and Homeostasis

The skin has multiple roles in homeostasis, including protection, control of body temperature, sensory reception, water balance, synthesis of vitamins and hormones, and absorption of materials. The skin's main functions are to serve as a barrier to the entry of microbes and viruses, and to prevent water and extracellular fluid loss. Acidic secretions from skin glands also stop the growth of fungi on the skin. Melanocytes form a second barrier: protection from the damaging effects of UV radiation. When a microbe gets into the skin (or when the skin is cut) an immune system reaction occurs.

Heat and cold receptors are located in the skin. When the body temperature rises, the hypothalamus sends a nerve signal to the sweat-producing skin glands, causing them to release sweat onto the skin surface. The evaporation of sweat helps reduce the temperature of the skin surface which cools the body. The hypothalamus also causes dilation of the blood vessels of the skin, allowing more blood to flow into those areas, causing heat to be released from the skin surface. When body temperature falls, the sweat glands constrict and sweat production decreases. If the body temperature continues to fall, the body will start to generate heat by raising the body's metabolic rate and by causing the muscles to shiver.

The homeostatic functions of the skin include:

- Protection of the body's internal tissues and organs.
- Protection against invasion by infectious organisms.
- Protection of the body from dehydration.
- Protection of the body against large changes in temperature.
- Excretion of wastes through sweat.
- Acts as a receptor for the senses of touch, pressure, pain, heat, and cold.
- Makes vitamin D through exposure to UV radiation.
- Stores water, fat, and vitamin D.

Homeostatic Imbalances of the Skin

Many wavelengths of electromagnetic radiation are emitted by the sun, some we can see, and others we cannot. The range of wavelengths of radiation we can see is called visible light. However, visible light makes up only a small portion of the total radiation that comes from the sun. Two other types of radiation that you have probably heard about before include infrared and ultraviolet radiation. Infrared light is the thermal energy, or the ‘‘heat rays” that you feel when the sun shines on you. The other, ultraviolet (UV), which we have discussed a little already, helps the body produce vitamin D, but it can also damage DNA in skin cells. Our main source of UV radiation, the sun, is shown in **Figure** 2.17.

Beneficial Effects of UV Radiation

A positive effect of ultraviolet radiation (UV) exposure is that it causes the production of vitamin D in the skin. It has been estimated that tens of thousands of premature deaths occur in the United States annually from a range of cancers due to vitamin D deficiency.

Ultraviolet radiation has other medical applications, in the treatment of skin conditions such as psoriasis, a disorder in which red, scaly patches form due to an overproduction of epithelial cells, and vitiligo, a condition that causes loss of pigment, which results in irregular pale patches of skin, as shown in **Figure** 2.18.

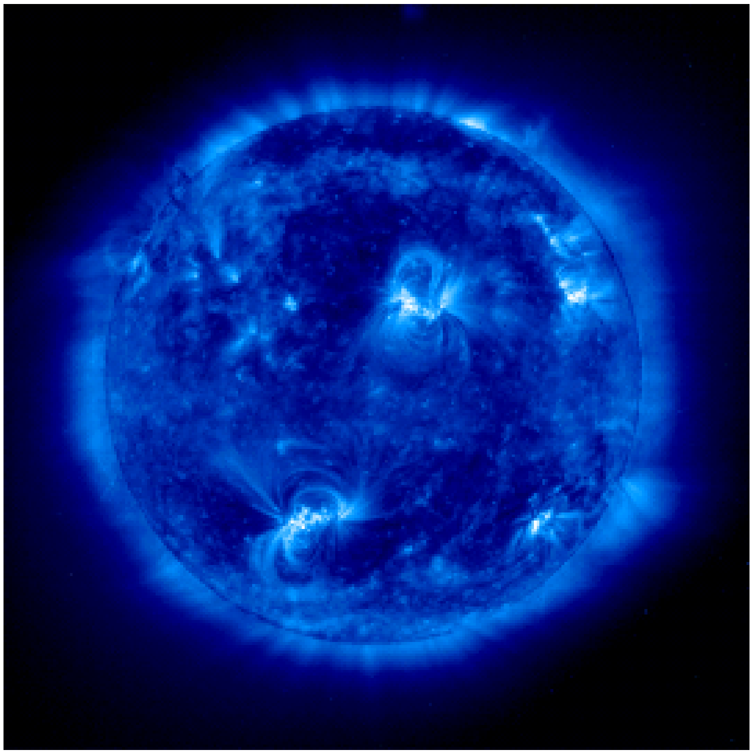

Figure 2.17: Ultraviolet radiation emitted by the sun. Prolonged exposure to UV radiation can lead to skin cancer and premature wrinkling of the skin.

Harmful Effects of UV Radiation

In humans, prolonged exposure to solar UV radiation may result in acute and chronic health effects on the skin, eye, and immune system. While some sunlight is good for health, skin cancer caused by excessive exposure to sunlight is not among the sun's benefits. Because some types of skin cancer are easy to cure, the danger posed by too much sunlight is perhaps not taken seriously enough. It is important to remember that a more serious form of skin cancer, called melanoma, is also associated with excessive sun exposure. Melanomas are potentially lethal tumors.

The UV radiation excites DNA molecules in skin cells, causing bonds to form between neighboring thymine bases, producing a thymine dimer that changes the shape of the DNA helix. These dimers can lead to mutations. **Mutations** are changes to the base pair sequence of DNA or RNA. Mutations can result in cancerous growths.

Skin cancer is an increasingly common condition. This is due in part to peoples' increased exposure to UV radiation, because of the increased popularity of sun bathing. Because melanin protects the skin from the effects of UV radiation, lighter-skinned people are at more risk of developing skin cancer than darker skinned people are. However, the risk of developing skin cancer is related to the amount of sunburn and overall length of time a person has been exposed to UV light. The three most common types of skin cancers are shown in **Figure** 2.19.

As a defense against UV radiation, the body tans when exposed to moderate levels of radiation by releasing the brown pigment melanin. This helps to block UV penetration and prevent damage to the vulnerable skin tissues deeper down. Suntan lotion, often referred to as "sun block" or "sunscreen", partly blocks UV and is widely available. Most of these products contain a sun protection factor (SPF) rating that describes the amount of protection given. This protection, however, applies only to a type of UV radiation

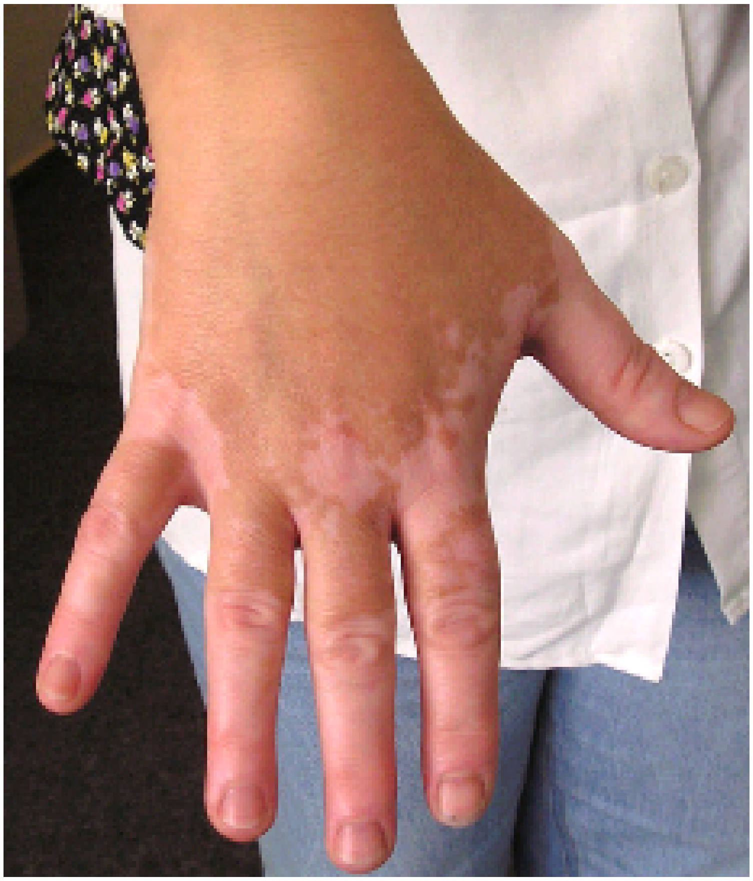

Figure 2.18: Vitiligo is chronic skin condition that causes loss of pigment, resulting in irregular pale patches of skin. The cause of vitiligo is not fully understood. There is some evidence suggesting it is caused by a combination of auto-immune, genetic, and environmental factors. Phototherapy in which the patient is exposed to long-wave ultraviolet (UVA) light from the sun or from UVA lamps, together with certain medicines, can help in many cases.

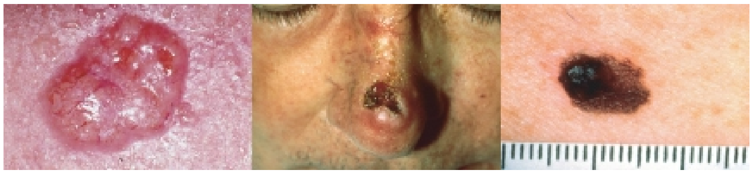

Figure 2.19: The three most common forms of skin cancer. Basal cell carcinoma (left), squamous cell carcinoma (center), and melanoma (right). All three types arise from cells in the epithelium.

called UVB rays, the type of radiation that is responsible for sunburn. UVA rays, another type of UV radiation, penetrates more deeply into the skin and may be responsible for causing cancer and wrinkles. Some sunscreen lotion now includes compounds such as titanium dioxide which helps protect against UVA rays. Other UVA blocking compounds found in sunscreen include zinc oxide and avobenzone. Another means to block UV is sun protective clothing, shown in **Figure** 2.20. This is clothing that has an ultraviolet protection factor (UPF) rating that describes the protection given against both UVA and UVB radiation.

Protect Yourself From Excessive Sunlight
SUN SCREEN
NATIONAL CANCER INSTITUTE

Figure 2.20: Some good advice from the National Cancer Institute. The risk of melanoma and other forms of skin cancer can be significantly reduced by avoiding excessive exposure to the sun, using sunscreen lotions, and wearing protective clothing to shield the skin from ultraviolet radiation.

Further Reading / Supplemental Links

- Anatomy and Physiology © 2002 Elaine Marieb. Published by Pearson Education Inc. as Benjamin Cummings.
- http://training.seer.cancer.gov/ss_module14_melanoma/unit02_sec01_anatomy
- http://www.estrellamountain.edu/faculty/farabee/biobk/BioBookINTEGUSYS
- http://www.cancer.gov/cancertopics/understandingcancer/environment
- http://www.cancer.gov/cancertopics/understandingcancer/cancer/Slide54
- http://animaldiversity.ummz.umich.edu/site/topics/mammal_anatomy/hair
- http://www.cancer.gov/cancertopics/understandingcancer/cancer
- http://www.cdc.gov/excite/skincancer/index
- http://www.niams.nih.gov/hi/topics/acne/acne
- http://en.wikipedia.org

Vocabulary

dermis The layer of skin directly under the epidermis, contains the hair follicles, sweat glands, sebaceous glands, and blood vessels.

epidermis The outermost layer of the skin.

integumentary system The organ system consisting of your skin, hair and nails.

melanin The brown pigment that gives skin, hair and eyes their color.

melanocytes Cells that produce melanin, found in the skin, hair and eyes.

mutation A change to the nucleotide sequence of DNA or RNA.

papillary region Part of the dermis that contains touch receptors, which communicate with the central nervous system.

reticular region Part of the dermis that contains the hair follicles and roots, nerves, and glands.

sebaceous gland Secretes an oily substance, called sebum, into the hair follicle.

sebum An oily substance secreted by sebaceous glands that is composed of lipids and debris of dead lipid-producing cells, responsible for protecting the skin and hair against drying out, and infection by microorganisms.

subcutaneous tissue (hypodermis) Lies below the dermis and contains fat and loose connective tissue that holds larger blood vessels and nerves, attaches the skin to underlying bone and muscle.

Points to Consider

- Identify reasons why you should wear sunblock with an SPF value of at least 15 everyday

Chapter 3

Circulatory, Lymphatic, and Re spiratory Systems

3.1 Circulatory System

Lesson Objectives

- Identify the functions and components of the cardiovascular system.
- Describe the structure of the heart.
- Outline the flow of blood through the heart.
- Compare the structures of arteries, veins, and capillaries.
- Compare pulmonary circulation and systemic circulation.
- Outline the functions of the lymphatic system.
- Describe the importance of the coronary arteries.
- Outline the process of atherosclerosis.
- Describe ways of preventing cardiovascular diseases.

Introduction

The **cardiovascular system** shown in **Figure** 3.1 is an organ system that moves nutrients, hormones, gases and wastes to and from body cells, and distributes heat to maintain homeostasis. The main components of the cardiovascular system are the heart, the blood vessels, and the blood.

The Heart

The **heart** is the muscular organ that pumps blood through the blood vessels by repeated, rhythmic contractions. The term cardiac means ”related to the heart” and comes from the Greek word *kardia*, for ”heart.” The heart is made up mostly of cardiac muscle tissue, (shown in **Figure** 3.2) which contracts to pump blood around the body. In adults, the normal mass of the heart is 250-350 grams (9-12 oz), or about three quarters the size of a clenched fist, but badly diseased hearts can be up to 1000 g (2 lb) in mass due to enlargement of the cardiac muscle. For an animation of the heart’s anatomy, see http://www.byrnehealthcare.com/animations/SutterAnatomy.htm.

The heart is usually found in the left to middle of the chest with the largest part of the heart slightly to

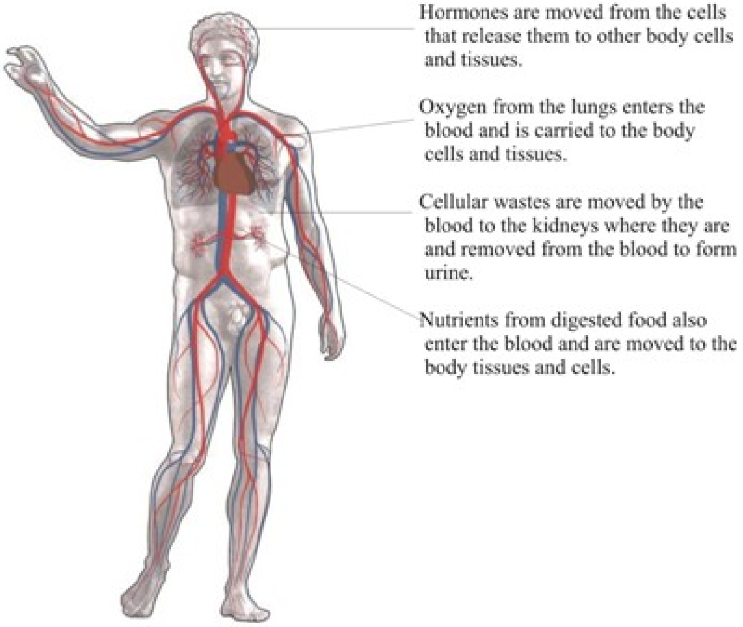
Hormones are moved from the cells that release them to other body cells and tissues.
Oxygen from the lungs enters the blood and is carried to the body cells and tissues.
Cellular wastes are moved by the blood to the kidneys where they are and removed from the blood to form urine.
Nutrients from digested food also enter the blood and are moved to the body tissues and cells.

Figure 3.1: The main organs of the circulatory system. Blood acts as the transporter in the body, while blood vessels act like little (one way) roads. The figure is Michelangelo

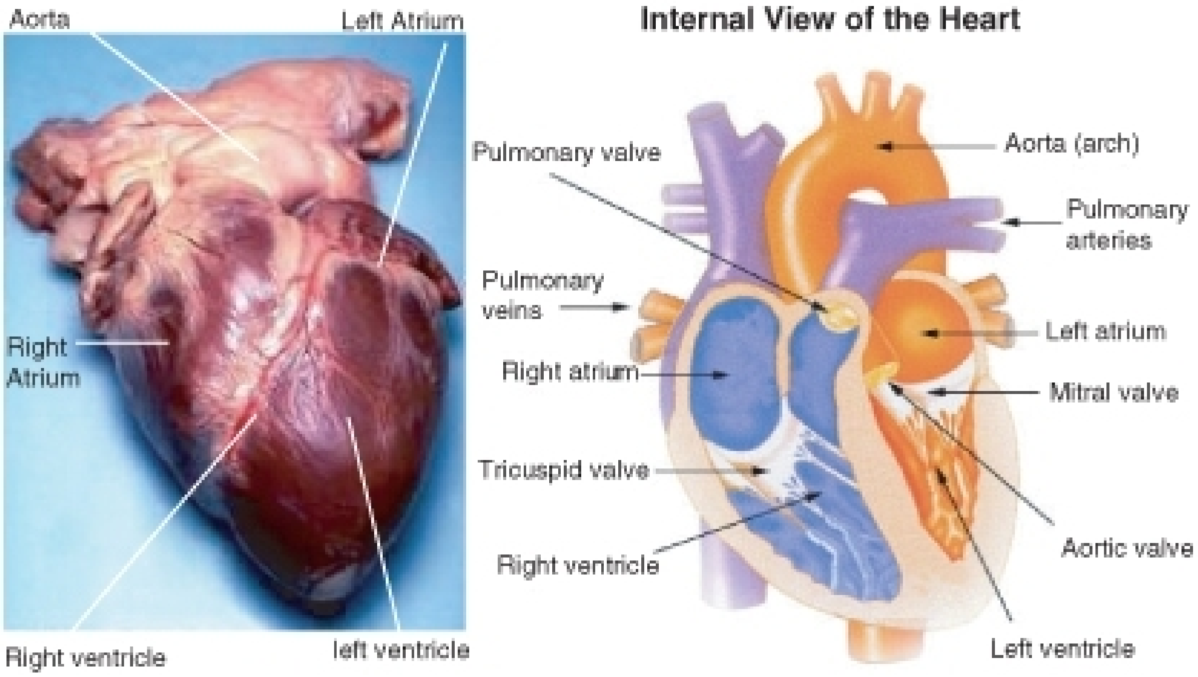

Figure 3.2: External and internal views of the human heart. The aorta in the photo cannot be seen clearly because it is covered by a layer of adipose tissue (fat).

the left. The heart is usually felt to be on the left side because the left ventricle is stronger (it pumps to all the body parts). The heart is surrounded by the lungs. The left lung is smaller than the right lung because the heart takes up more room in the left side of the chest. The position of the heart within the chest is shown in **Figure** 3.3.

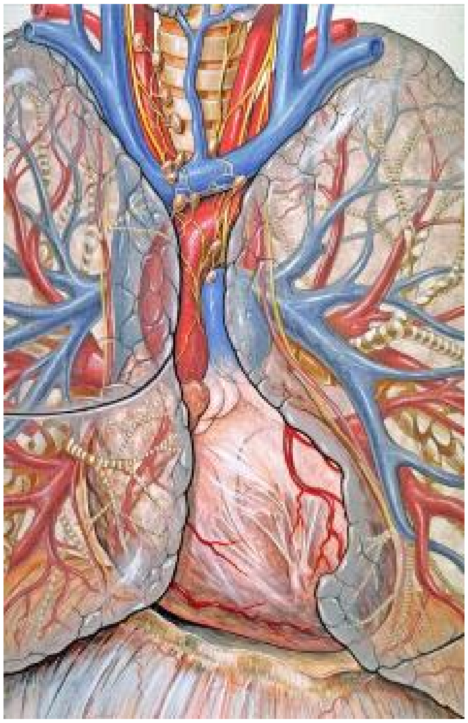

Figure 3.3: Position of the heart in relation to the lungs. The heart can be seen in the lower middle area of the figure, behind the lungs.

Blood Flow Through the Heart

Blood flows through the heart in two separate loops; you could think of them as a “left side loop” and a “right side loop.” The right side and left side of the heart refer to your heart as it sits within your chest. Its left side is your left side and, its right side is your right side.

The right side of the heart collects deoxygenated blood from the body and pumps it into the lungs where it releases carbon dioxide and picks up oxygen. The left-side carries the oxygenated blood back from the lungs, into the left side of the heart which then pumps the oxygenated blood throughout the rest of the body.

The heart has four chambers, the two upper atria and the two lower ventricles. **Atria** (singular, atrium) are the thin-walled blood collection chambers of the heart. Atria pump the blood into the ventricles. **Ventricles** are the heart chambers which collect blood from the atria and pump it out of the heart. On the right side of the heart, deoxygenated blood from the body enters the right atrium from the superior vena cava and the inferior vena cava, shown in **Figure** 3.4. Blood enters the right ventricle which then pumps the blood through the pulmonary arteries and into the lungs. In the lungs, carbon dioxide is released from the blood and oxygen is picked up.

Pulmonary veins bring the oxygenated blood back to the heart and into the left atrium. From the left atrium the blood moves to the left ventricle which pumps it out to the body through the aorta. On both sides, the lower ventricles are thicker and stronger than the upper atria. The muscle wall surrounding the left ventricle is thicker and stronger than the wall surrounding the right ventricle because the left ventricle needs to exert enough force to pump the blood through the body. The right ventricle only needs to pump the blood as far as the lungs, which does not require as much contractile force.

Valves in the heart maintain the flow of blood by opening and closing in one direction only. Blood can move only forward through the heart, and is prevented from flowing backward by the valves. Such movement of the blood is called unidirectional flow. There are four valves of the heart:

- The two **atrioventricular (AV) valves** ensure blood flows from the atria to the ventricles, and not the other way. The AV valve on the right side of the heart is called the tricuspid valve, and the one on the left of the heart is called the mitral, or bicuspid valve.
- The two **semilunar (SL) valves** are present in the arteries leaving the heart, and they prevent blood flowing back from the arteries into the ventricles. The SL valve on the right side of the heart is called the pulmonary valve, because it is leads to the pulmonary arteries, and the SL valve on the left is called aortic valve because it leads to the aorta. The valves of the heart are shown in **Figure** 3.4.

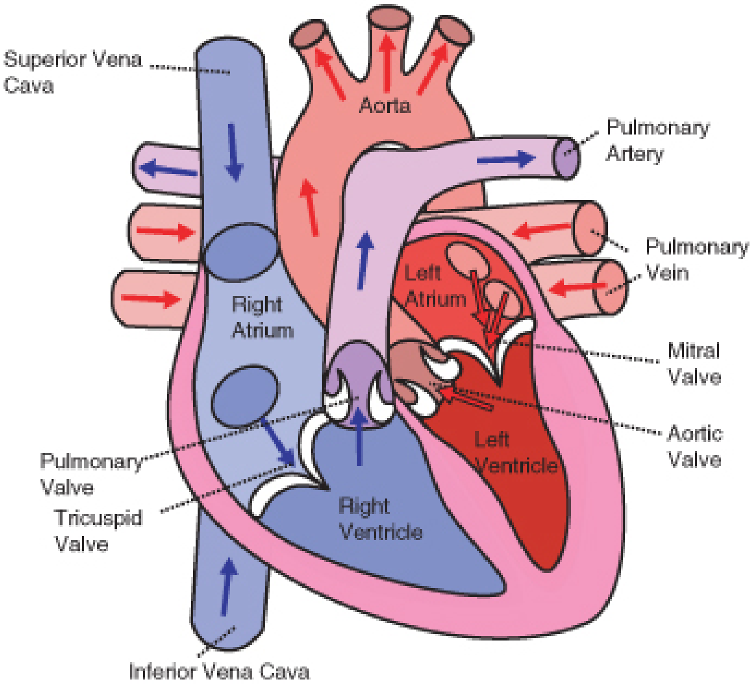

Figure 3.4: The direction of blood flow through the heart.

The Heartbeat

The heart is a meshwork of cardiac muscle cells that are interconnected by little channels called gap junctions. This interconnection allows the electrical stimulation of one cell to spread quickly to its neighboring cells. Cardiac muscle is self-exciting. This is in contrast to skeletal muscle, which needs nervous stimulation to contract. The heart's rhythmic contractions occur spontaneously, although the frequency of the contractions, called the **heart rate**, can be changed by nervous or hormonal signals such as exercise or the perception of danger.

Control of the Heartbeat

The rhythmic sequence of contractions of the heart is coordinated by two small groups of cardiac muscle cells called the sinoatrial (SA) and atrioventricular (AV) nodes. The **sinoatrial node (SA node)**, often known as the ”cardiac pacemaker”, is found in the upper wall of the right atrium and is responsible for the wave of electrical stimulation that starts atrial contraction by creating an action potential. The action potential causes the cardiac cells to contract. This wave of contraction then spreads across the cells of the atrium, reaching the **atrioventricular node (AV node)** which is found in the lower right atrium, shown in **Figure** 3.5. The AV node conducts the electrical impulses that come from the SA node through the atria to the ventricles. The impulse is delayed there before being conducted through special bundles of heart muscle cells called the bundle of His and the Purkinje fibers, which leads to a contraction of the ventricles. This delay allows for the ventricles to fill with blood before the ventricles contract. Heartbeat is also controlled by nerve messages originating from the autonomic nervous system.

There are important physiological differences between cardiac cells found in the nodes and cardiac cells found in the ventricles. Differences in ion channels and mechanisms of polarization give rise to unique properties of SA node cells, most importantly the spontaneous depolarizations necessary for the SA node’s pacemaker activity.

The **Bundle of His** is a collection of heart muscle cells (fibers) specialized for electrical conduction that transmits the electrical impulses from the AV node. The bundle of His branches into Purkinje fibers. **Purkinje fibers**, shown in **Figure** 3.6, are specialized cardiac muscle cells that conduct action potentials into the ventricles, causing the cardiac muscle of the ventricles to contract in a controlled way.

The heartbeat is made up of two parts; muscle contraction and relaxation. **Systole** is the contraction of the heart chambers, which drives blood out of the chambers. **Diastole** is the period of time when the heart relaxes after contraction. All four chambers of the heart undergo systole and diastole in a timed fashion so that blood is moved forward through the cardiovascular system. For example, ventricular systole is the point at which the ventricles are contracting, and atrial systole is the point at which the atria are contracting. Likewise, ventricular diastole is the period during which the ventricles are relaxing, while atrial diastole is the period during which the atria are relaxing. In general, when referring to systole and diastole, the chambers being referred to are the ventricles, which is shown in **Figure** 3.7.

Another animation of how the blood flows through the heart from Nova: http://www.pbs.org/wgbh/nova/heart/heartmap.html

Heart Sounds

In healthy adults, there are two normal heart sounds often described as a ”lub” and a ”dub” that occur with each heart beat (lub-dub, lub-dub). In addition to these normal sounds, a variety of other sounds may be heard including heart murmurs or clicks. A medical practitioner uses a stethoscope to listen for these sounds, which gives him or her important information about the condition of the heart.

The sound of the heart valves shutting causes the heart sounds, or a heartbeat. The closing of the mitral and tricuspid valves (known together as the atrioventricular valves) at the beginning of ventricular systole cause the first part of the ”lub-dub” sound made by the heart as it beats. The second part of the ”lub-dub” is caused by the closure of the aortic and pulmonic valves at the end of ventricular systole. As the left ventricle empties, its pressure falls below the pressure in the aorta, and the aortic valve closes. Similarly, as the pressure in the right ventricle falls below the pressure in the pulmonary artery, the pulmonic valve closes.

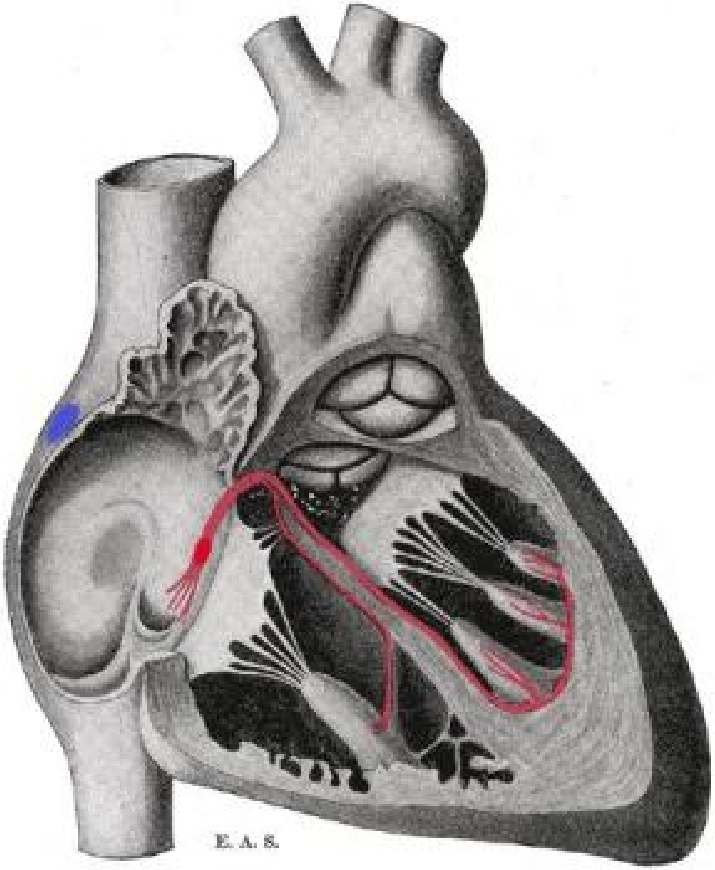

Figure 3.5: Schematic representation of the atrioventricular Bundle of His. The SA node is blue, and the AV node is red and visible in the right atrium. The AV node forms the Bundle of His. Sometimes the left and right Bundles of His are called Purkinje fibers.

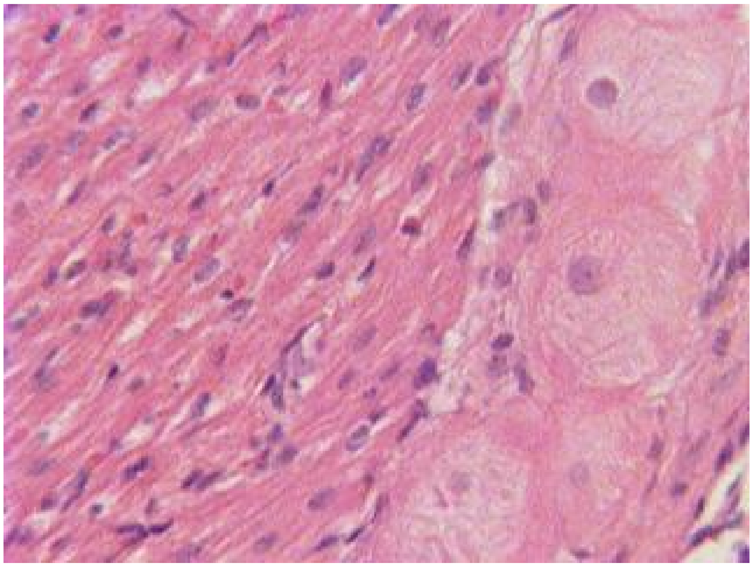

Figure 3.6: The larger round cells on the right are Purkinje fibers. Because of their specializations to rapidly conduct impulses (numerous sodium ion channels and mitochondria, fewer myofibrils than the surrounding muscle tissue), Purkinje fibers take up stain differently than the surrounding muscles cells, and on a slide, they often appear lighter and larger than their neighbors.

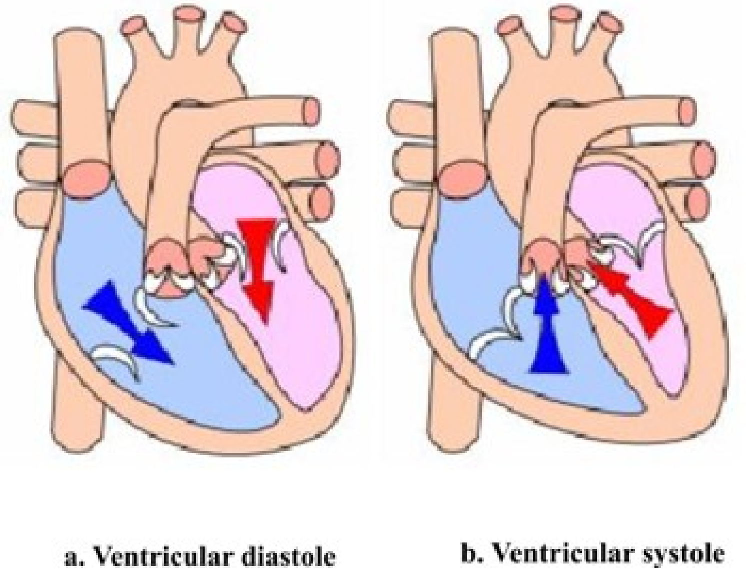

Figure 3.7: When the atria contract, the blood gets pushed into the ventricles which are in diastole. When the ventricles contract (ventricular systole), the blood gets pushed out of the heart.

Figure 3.8: medical animation beating heart (Watch Youtube Video)
http://www.ck12.org/flexbook/embed/view/482

Blood Vessels

The blood vessels are part of the cardiovascular system and function to transport blood throughout the body. The two most important types are arteries and veins. Arteries carry blood away from the heart, while veins return blood to the heart.

There are various kinds of blood vessels, the main types are:

- **Arteries** are the large, muscular vessels that carry blood away from the heart.
- An **arteriole** is a small diameter blood vessel that extends and branches out from an artery and leads to capillaries.
- **Veins** are vessels that carry blood toward the heart. The majority of veins in the body carry low-oxygen blood from the tissues back to the heart.
- A **venule** is a small vessel that allows deoxygenated blood to return from the capillaries to veins.
- **Capillaries** are the smallest of the body's blood vessels, that connect arterioles and venules, and are important for the interchange of gases and other substances between blood and body cells.

The blood vessels have a similar basic structure. The **endothelium** is a thin layer of cells that creates a smooth lining on the inside surface of blood vessels. Endothelial tissue is a specialized type of epithelium, one of the four types of tissue found in the body. Endothelial cells have an important structural role in blood vessels; they line the entire circulatory system, from the heart to the smallest capillary. Around the endothelium there is a layer of smooth muscle, which is well developed in arteries. Finally, there is a further layer of connective tissue that surrounds the smooth muscle. This connective tissue, which is mostly made up of collagen, contains nerves that supply the smooth muscular layer. The connective tissue surrounding larger vessels also contains capillaries to bring nutrients to the tissue. Capillaries, the smallest blood vessels, are made up of a single layer of endothelium and a small amount of connective tissue.

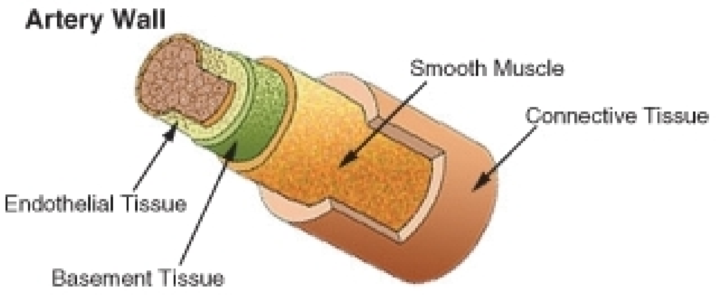

Figure 3.9: The structure of an artery wall.

Roles of Blood Vessels

Blood vessels are not involved in regulating the transport of blood, the endocrine and nervous systems do that. However, arteries and veins can regulate their inner diameter by contraction of the smooth muscle layer. This widening or narrowing of the blood vessels changes the blood flow to the organs of the body. This process is controlled by the autonomic nervous system; it is not controlled consciously.

Vasodilation is a process by which blood vessels in the body become wider due to the relaxation of the smooth muscle in the vessel wall. This reduces blood pressure since there is more room for the blood to move through the vessel. Endothelium of blood vessels uses nitric oxide to signal the surrounding smooth muscle to relax, which dilates the artery and increasing blood flow. Nitric dioxide is a vasodilator.

Vasoconstriction is the constriction of blood vessels (narrowing, becoming smaller in cross-sectional area) by contracting the vascular smooth muscle in the vessel walls. Vasoconstriction is controlled by substances such as some hormones and neurotransmitters, which are called vasoconstrictors. For example, the “fight or flight” hormone epinephrine is a vasoconstrictor that is released by the adrenal glands.

Permeability of the endothelium is important for the release of nutrients to the tissue. Permeability is the ability of a membrane to allow certain molecules and ions to pass through it by diffusion. Permeability of the endothelium increases during an immune response, which allows white blood cells and other substances to get to the site of injury or irritation.

Oxygen, which is bound to hemoglobin in red blood cells for transport through the body, is the most critical nutrient carried by the blood. In all arteries apart from the pulmonary artery, hemoglobin is highly saturated (95-100%) with oxygen. In all veins apart from the pulmonary vein, the hemoglobin is desaturated at about 70%. (The values are reversed in the pulmonary circulation.)

Blood Vessels and Blood Pressure

Blood pressure refers to the force exerted by circulating blood on the walls of blood vessels. The pressure of the circulating blood gradually decreases as blood moves from the arteries, arterioles, capillaries, and veins. The term ”blood pressure” generally refers to **arterial pressure**, which is the pressure in the larger arteries that take blood away from the heart. Arterial pressure results from the force that is applied to blood by the contracting heart, where the blood “presses” against the walls of the arteries.

The systolic arterial pressure is defined as the peak pressure in the arteries, which occurs near the beginning of the cardiac cycle; the diastolic arterial pressure is the lowest pressure (at the resting phase of the cardiac cycle).

Arterial pressure is most commonly measured by a **sphygmomanometer**, shown in **Figure** 3.10. The height of a column of mercury indicates the pressure of the circulating blood. Although many modern blood pressure devices no longer use mercury, values are still universally reported in millimeters of mercury (mmHg).

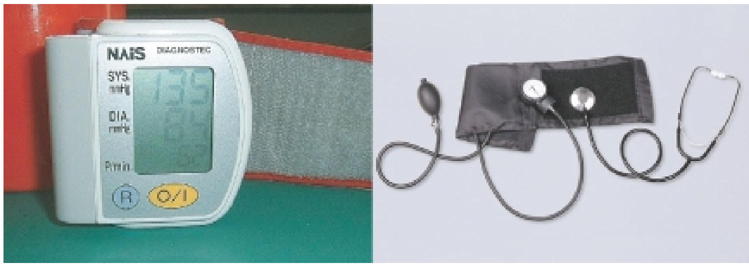

Figure 3.10: The new and the

Blood Pressure Ranges

In the U.S., the healthy ranges for arterial pressure are:

- Systolic: less than 120 mm Hg
- Diastolic: less than 80 mm Hg

Blood pressure is usually written as systolic/diastolic mm Hg; for example, a reading of 120/80 mm Hg, is said as ”one twenty over eighty.” These measures of arterial pressure are not static, but go through natural variations from one heartbeat to another and throughout the day (in a circadian rhythm). Factors such as age, gender and race influence blood pressure values. Pressure also varies with exercise, emotional reactions, sleep, stress, nutritional factors, drugs, or disease.

Studies have shown that people whose systolic pressure is around 115 mm Hg rather than 120 mmHg have fewer health problems. Clinical trials have shown that people who have arterial pressures at the low end of these ranges have much better long term cardiovascular health for this reason some researchers say that 115/75 mm Hg should be the ideal measurement.

Hypertension is a condition in which a person’s blood pressure is chronically high. Hypertension is said to be present when a person’s systolic blood pressure is always 140 mm Hg or higher, and/or their diastolic blood pressure is always 90 mm Hg or higher. Blood pressure readings between 120/80 mmHg and 139/89 mmHg are called prehypertension. Prehypertension is not a disease category; rather, it is a way to identify people who are at high risk of developing hypertension.

Arterioles and Blood Pressure

Arterioles have the greatest collective influence on both local blood flow and on overall blood pressure. They are the primary ”adjustable nozzles” in the blood system, across which the greatest pressure drop occurs. The combination of heart output (cardiac output) and systemic vascular resistance, which refers to the collective resistance of all of the body’s arterioles, are the principal determinants of arterial blood pressure at any given moment.

Pulmonary and Systemic Circulations

The double circulatory system of blood flow refers to the separate systems of pulmonary circulation and the systemic circulation in amphibians, birds and mammals, including humans. The adult human heart consists of two separated pumps, the right side which pumps deoxygenated blood into the pulmonary circulation, and the left side which pumps oxygenated blood into the systemic circulation. Blood in one circuit has to go through the heart to enter the other circuit, as shown in **Figure** 3.11.

Pulmonary Circulation

The **pulmonary circulation** is the portion of the cardiovascular system which carries oxygen-poor (deoxygenated) blood away from the heart, to the lungs, and returns oxygenated blood back to the heart. As shown in **Figure** 3.12, deoxygenated blood from the body leaves the right ventricle through the pulmonary arteries, which carry the blood to each lung. The pulmonary arteries are the only arteries that carry deoxygenated blood. In the lungs, red blood cells release carbon dioxide and pick up oxygen during respiration. The oxygenated blood then leaves the lungs through the pulmonary veins, which return it to the left side of the heart, and complete the pulmonary cycle. The oxygenated blood is then distributed to the body through the systemic circulation before returning again to the pulmonary circulation.

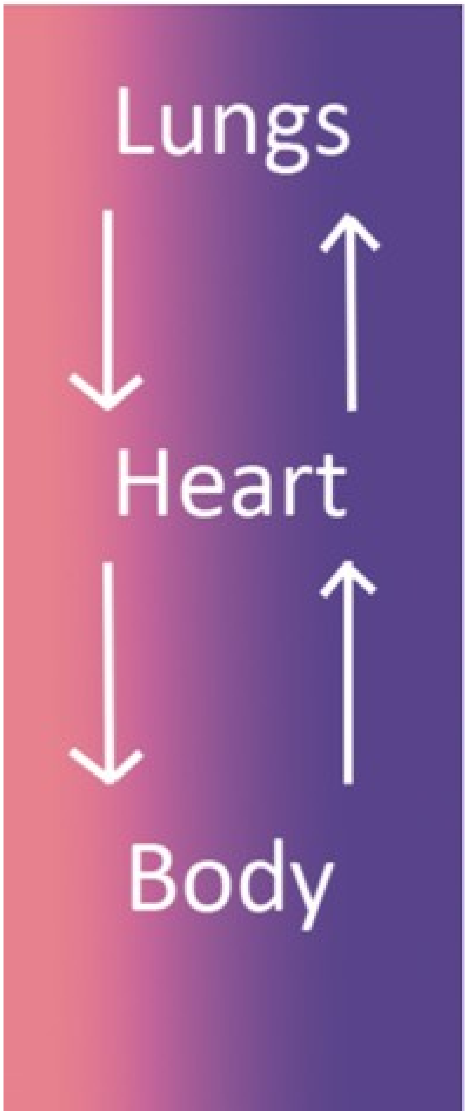

Figure 3.11: The double circulatory system. Blood in one circuit has to go through the heart to enter the other circuit. The heart-to-lungs-to heart portion is the pulmonary circulation, and the heart-to-body-to-heart portion is the systemic circulation.

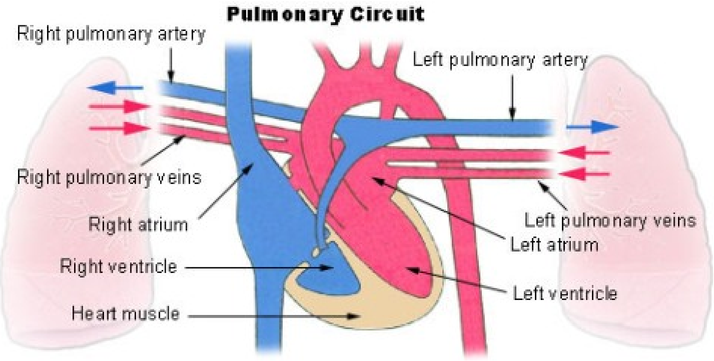

Figure 3.12: Pulmonary circulation. The pulmonary arteries carry oxygen-poor blood from the right ventricle to the lungs, and the pulmonary veins return oxygenated blood to the left side of the heart. This

The pulmonary circulation was first discovered by a Syrian physician, Ibn al-Nafis, in 1242. However, credit for the first description of blood circulation is given to an English medical doctor William Harvey, who in 1616 described in detail the pulmonary and systemic circulation systems.

Systemic Circulation

The **systemic circulation** is the portion of the cardiovascular system which carries oxygenated blood away from the heart, to the body, and returns deoxygenated blood back to the heart. Oxygenated blood from the lungs leaves the left ventricle through the aorta, from where it is distributed to the body's organs and tissues, which absorb the oxygen, through a complex network of arteries, arterioles, and capillaries. The deoxygenated blood is then collected by venules, from where it flows first into veins, and then into the inferior and superior venae cavae, which return it to the right heart, completing the systemic cycle, shown in **Figure** 3.13. The blood is then re-oxygenated through the pulmonary circulation before returning again to the systemic circulation.

Just like every other organ in the body, the heart needs its own blood supply, which it gets through the **coronary circulation**. Although blood fills the chambers of the heart, the heart muscle tissue is so thick that it needs blood vessels to deliver oxygen and nutrients deep within it. The vessels that deliver oxygen-rich blood to the heart muscle are called coronary arteries, they branch directly from the aorta, just above the heart, shown in **Figure** 3.14. The vessels that remove the deoxygenated blood from the heart muscle are known as cardiac veins.

Portal Venous System

A **portal venous system** occurs when a capillary bed drains into another capillary bed through veins. They are relatively uncommon as the majority of capillary beds drain into the heart, not into another capillary bed. Portal venous systems are considered venous because the blood vessels that join the two capillary beds are either veins or venules.

An example of a portal venous system is the blood vessel network between the digestive tract and the liver. The hepatic portal system is responsible for directing blood from parts of the gastrointestinal tract to the liver. Nutrients that have been absorbed into the blood from the small intestine are taken to the liver for processing before being sent to the heart. The term, ”portal venous system” often refers to the hepatic portal system.

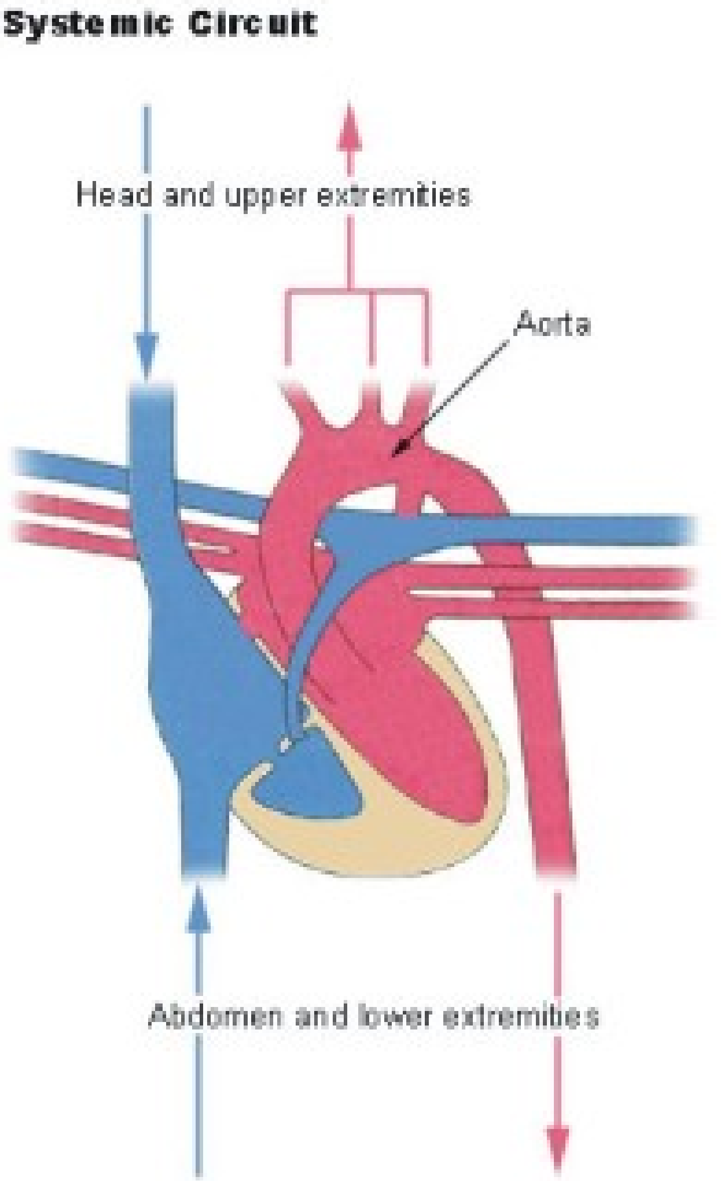

Figure 3.13: The systemic circulation. The systemic circulation brings oxygenated blood to the body cells and tissues and transports cellular wastes. It is also responsible for temperature regulation and transport of hormones and other substances around the body.

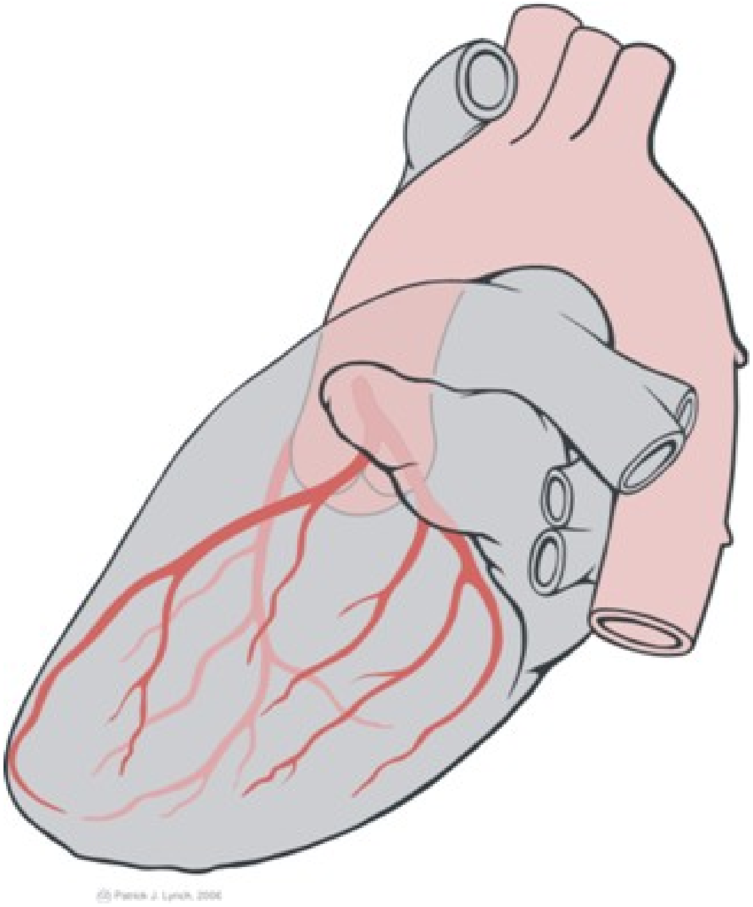

Figure 3.14: This side view (lateral view), of the heart shows how the coronary arteries (in red) branch directly from the aorta to bring oxygen and nutrients into the heart muscle.

3.2 Lymphatic System

The **lymphatic system**, shown in **Figure** 3.15, is a complex network of lymph nodes, lymph ducts, lymphatic tissues, lymph capillaries and lymph vessels that extend the length of the body. It serves as a conduit for a fluid called lymph. The lymphatic system is often called the secondary circulatory system.

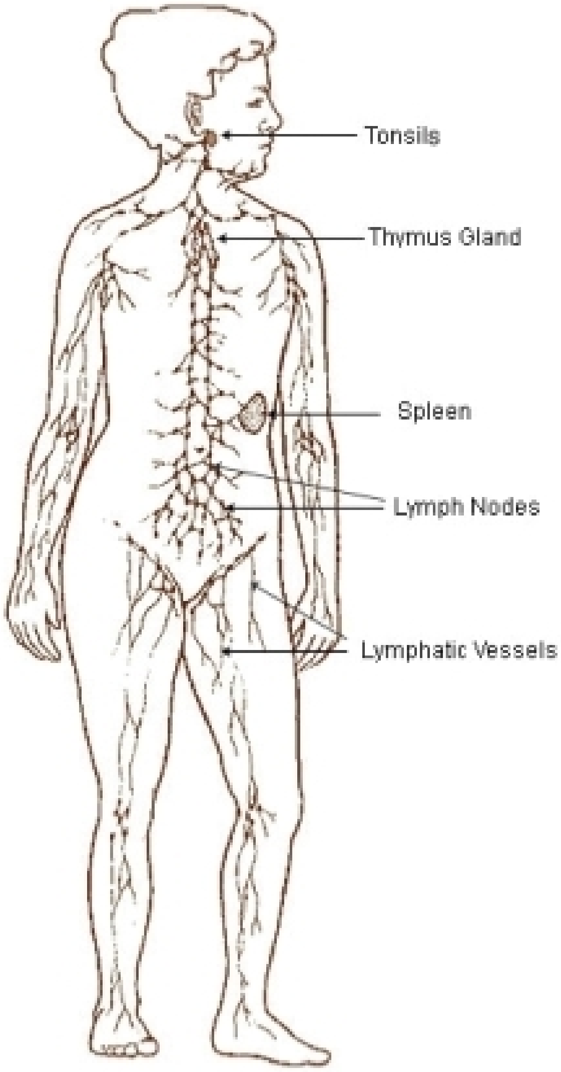

Figure 3.15: Lymphatic system

The lymphatic system has three related functions:

- The removal of excess fluids from body tissues.
- The absorption of fats, also known as fatty acids or lipids, and transport of fats to the cardiovascular system.
- The production of certain types of white blood cells, which aid in the body's immune response.

Lymph originates as blood plasma that leaks from the capillaries of the cardiovascular system. This blood plasma fills the space between individual cells of tissue where it becomes part of the interstitial fluid. Plasma is forced out of the capillaries and forced back in due to interactions of hydrostatic pressure. While out of the blood capillaries, the plasma increases the volume of the interstitial fluid. Most of the interstitial fluid is returned to the capillaries by osmosis. The excess interstitial fluid is collected by the lymphatic system by diffusion into **lymph capillaries**, and is processed by lymph nodes before to being returned to the circulatory system. Once within the lymphatic system the fluid is called lymph, and has almost the same composition as the original interstitial fluid.

Fatty acids, also known as fats or lipids, are transported through the cardiovascular system differently than other nutrients, such as proteins and sugars. Lipids are absorbed by cells in the villi of the small intestine where they form a complex with protein molecules. These lipo-proteins are called **chylomicrons**. The chylomicrons are transported via the lymphatic system and eventually rejoin the bloodstream to be processed by the liver.

The lymphatic system is a major component of the immune system. The lymphatic system has many lymph nodes. **Lymph nodes** are filters or traps for foreign particles and contain white blood cells. Human lymph nodes are bean-shaped and range in size from a few millimeters to about 1 to 2 cm. White blood cells are located within honeycomb structures of the lymph nodes. Lymph that moves through the lymph nodes is filtered so that microorganisms and tissue debris are removed. Lymph nodes swell and feel sore when the body is infected due to the increased production of white blood cells.

The spleen and tonsils are large lymphoid organs that serve similar functions to lymph nodes, though the spleen filters blood cells rather than bacteria or viruses.

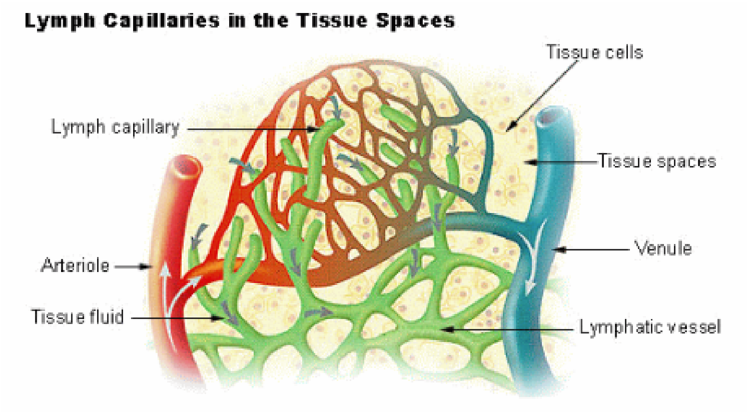

Figure 3.16: The movement of lymph from the interstitial fluid into the lymphatic vessels. Lymph moves in only one direction through the blood vessels.

Lymphatic Circulation

Unlike the blood system, the lymphatic system is not closed and has no central pump. Lymph movement occurs slowly with low pressure due to peristalsis, valves, and the squeezing action of skeletal muscles. Lymph travels through lymph vessels that are similar to capillaries and veins. Lymph moves in one direction only, due to valves in lymph vessels that are similar to the valves found in veins, shown in **Figure** 3.16. The movement of lymph depends on the movement of skeletal muscles to squeezing the lymph through them, especially near the joints. Rhythmic contraction of the vessel walls through movements may also help draw fluid into the small lymphatic capillaries. The lymph is then transported to progressively larger lymphatic vessels that drain into the circulatory system at the right and left subclavian veins.

Homeostatic Imbalance of the Lymphatic System

In the disease known as elephantiasis, shown in **Figure** 3.17, infection of the lymphatic vessels cause a thickening of the skin and enlargement of the underlying tissues, especially in the legs and genitals. It is most commonly caused by infection by parasitic roundworms.

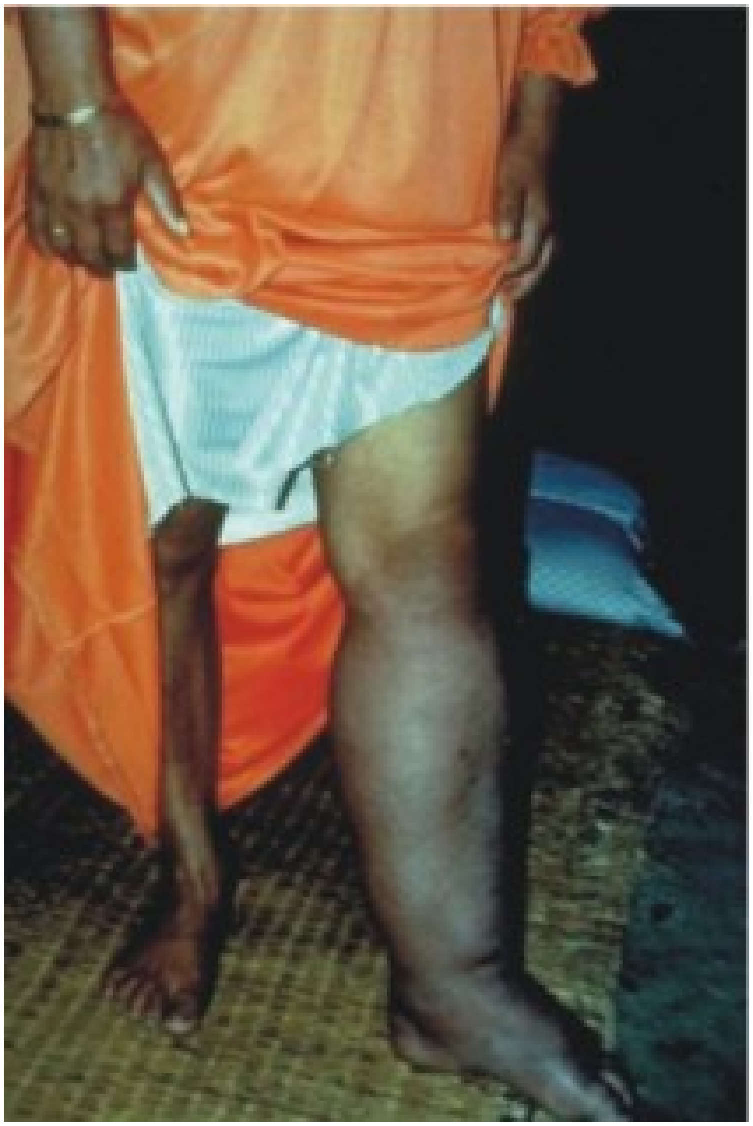

Figure 3.17: Over a billion people are at risk for infection by filarial nematodes, the parasites that cause elephantiasis.

Lymphedema also causes abnormal swelling, especially in the arms and legs (though the face, neck, and abdomen can also be affected). It occurs if the lymphatic system is damaged, or underdeveloped in some way. An estimated 170 million suffer with the disorder.

Lymphoma, or lymphatic cancer, is cancer of the lymphatic system. According to the American Cancer Society, in 2007, lymphoma accounted for 4 percent of new cancer cases amongst men and women in the United States. In lymphoma, cells of the lymphatic system grow abnormally. They divide too rapidly and grow without any order or control. Because lymphatic tissue is present in many parts of the body, lymphoma can start almost anywhere. Lymphoma may occur in a single lymph node, a group of lymph nodes, or, sometimes, in other parts of the lymphatic system such as the bone marrow and spleen.

Homeostatic Imbalances of the Cardiovascular System

Cardiovascular disease (CVD) refers to any disease that affects the cardiovascular system, but it is usually used to refer to diseases related to **atherosclerosis**, which is a chronic inflammatory response in the walls of arteries that causes a swelling and buildup of materials called **plaque**. Plaque is made of cell debris, cholesterol, fatty acids, calcium, and fibrous connective tissue that build up around an area of inflammation. As a plaque grows it stiffens and narrows the artery, which reduces the flow of blood through the artery, shown in **Figure** 3.18.

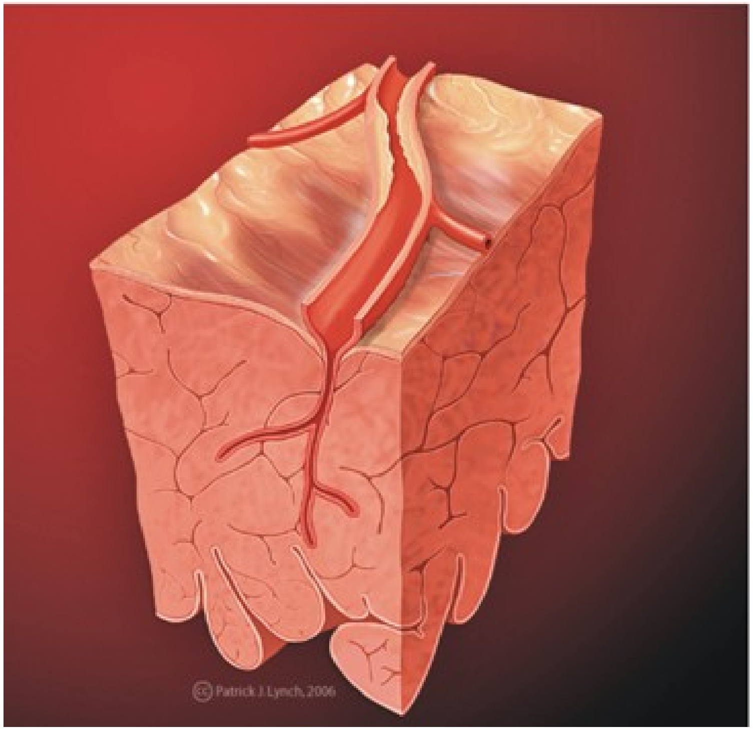

Figure 3.18: Atherosclerosis is sometimes referred to as hardening of the arteries.

Atherosclerosis

Atherosclerosis normally begins in later childhood, and is usually found in most major arteries. It does not usually have any early symptoms. Causes of atherosclerosis include a high-fat diet, high cholesterol, smoking, obesity, and diabetes. Atherosclerosis becomes a threat to health when the plaque buildup interferes with the blood circulation in the heart (coronary circulation) or the brain (cerebral circulation). A blockage in the coronary circulation, can lead to a heart attack, and blockage of the cerebral circulation (leading to, or within the brain) can lead to a stroke. According to the American Heart Association, atherosclerosis is a leading cause of CVD.

Coronary Heart Disease

Cardiac muscle cells are fed by the coronary arteries. Blocked flow in a coronary artery can result in oxygen starvation and death of heart muscle. **Coronary heart disease** is the end result of the buildup of plaques within the walls of the coronary arteries, shown in **Figure** 3.19. Most individuals with coronary heart disease have no symptoms for many years until the first sign, often a heart attack, happens.

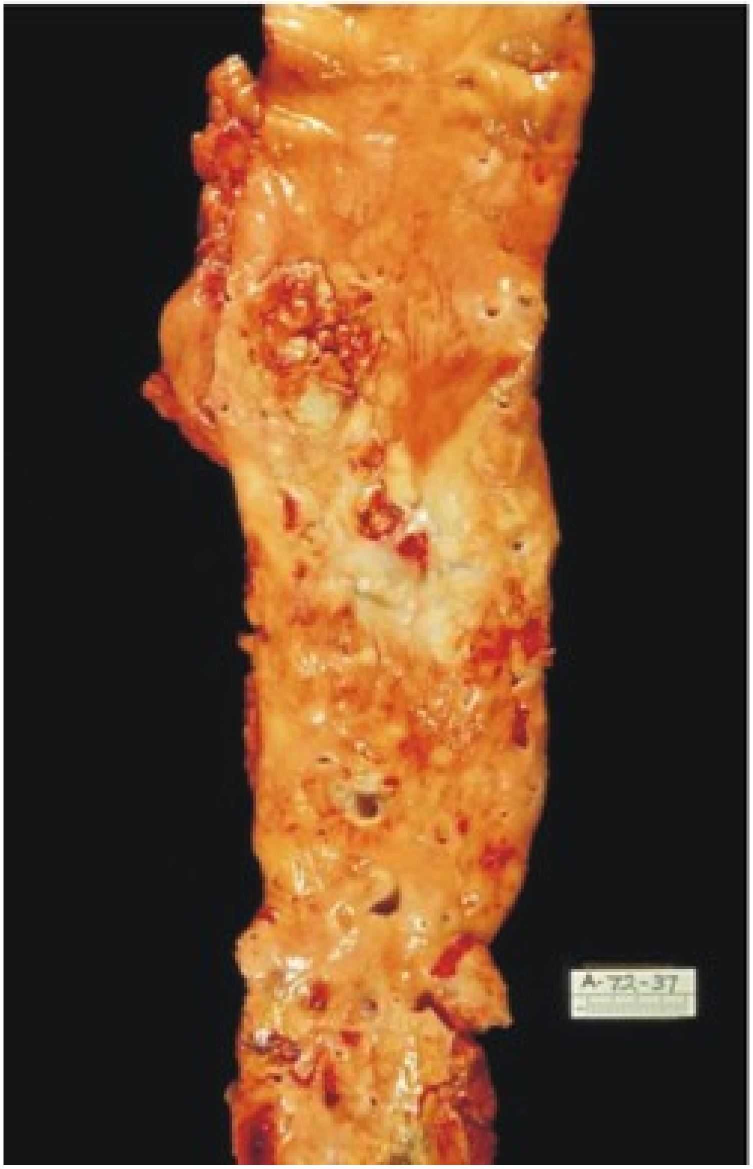

Figure 3.19: Autopsy specimen of an artery has been opened lengthwise to show the inside (lumen) which is completely blocked by many plaques. For a video depicting atherosclerosis, see

A symptom of coronary heart disease is chest pain. Occasional chest pain, called angina pectoralis (or angina) can happen during times of stress or physical exertion. The pain of angina means the heart muscle fibers need more oxygen than they are getting.

A **heart attack**, also called a **myocardial infarction (MI)**, occurs when the blood supply to a part of the heart is blocked, as shown in **Figure** 3.20. A heart attack can occur from the buildup and blockage of a coronary artery by plaque, or it can be caused by a small piece of plaque that breaks away when a larger plaque breaks apart. This piece of free-floating plaque, called an embolus, can get stuck in a coronary blood vessel, causing a blockage or **embolism**. Cardiac muscle fibers that are starved of oxygen for more than five minutes will die, and because they do not divide, dead cardiac muscle cells cannot be replaced. Coronary heart disease is the leading causes of death of adults in the United States. For an animation depicting a heart attack, see http://www.byrnehealthcare.com/animations/SutterHeartAttack.htm.

Stroke

Since atherosclerosis is a body wide process, similar events can also occur in the arteries to other parts of the body, including the brain. A **stroke** is a loss of brain function due to a stoppage of the blood supply to the brain. It can be caused by a blot clot (thrombosis), a free-floating object that gets caught in a blood vessel (embolism), or by bleeding (hemorrhage). For an animation depicting a stroke, see http://www.byrnehealthcare.com/animations/SutterStroke.htm.

Risk factors for stroke include advanced age, high blood pressure, previous stroke, diabetes, high cholesterol, and cigarette smoking. Reduction of blood pressure is the most important modifiable risk factor of stroke; however many other risk factors, such as quitting tobacco smoking, are also important.

Preventing Cardiovascular Diseases

There are many risk factors which are associated with various forms of cardiovascular disease, some of these you cannot control, but many you can control.

Non-controllable risk factors include:

- Age: The older a person is, the greater their chance of developing a cardiovascular disease.
- Gender: Men under age 64 are much more likely to die of coronary heart disease than women, although the gender difference declines with age.
- Genetics: Family history of cardiovascular disease affects a person's chance of developing heart disease.

Controllable risk factors include:

- Tobacco Smoking: Giving up smoking is the single most effective way of reducing risk of heart disease.
- Diabetes: Having diabetes can cause metabolic changes (such as high cholesterol levels) which in themselves are risk factors.
- High cholesterol levels: High amounts of low density lipids (LDLs) in the blood, also called ”bad cholesterol”, are a significant risk factor.
- Obesity: Being obese, especially if the fat is deposited mostly in the torso, rather than the hips and thighs, increases risk significantly.
- High blood pressure: Hypertension can cause atherosclerosis.
- Lack of physical activity: Aerobic activities, including walking and vacuuming, that are done for 60 minutes a day, five days a week, help keep the heart healthy.

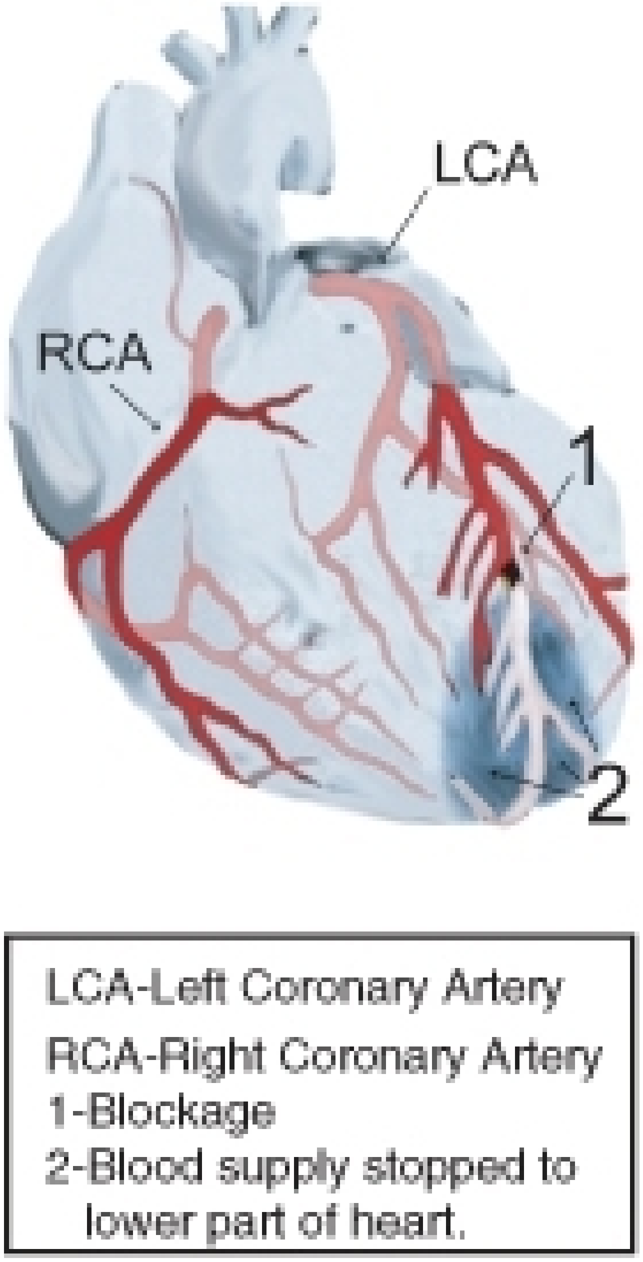
LCA
RCA
1
2
LCA-Left Coronary Artery
RCA-Right Coronary Artery
1-Blockage
2-Blood supply stopped to lower part of heart.

Figure 3.20: Diagram of a heart attack (myocardial infarction). The blood supply to the lower part of the heart is stopped after a blockage of the lower portion of the left coronary artery (LCA). For an animation depicting coronary artery disease, see

- Poor eating habits: Eating mostly foods that are nutrient poor (do not have many nutrients other than fat or carbohydrate) leads to high cholesterol levels and weight gain, among other things.

Although there are uncontrollable risk factors involved in CVD, a person whose family has a history of CVD is not destined to develop heart disease. There are many things such a person can do to help prevent CVD, even when predisposed to a disease. A person who is physically active every day, eats healthfully, and avoids tobacco can lower their chances of developing the disease.

Although men have a higher rate of cardiovascular disease than women, it is also the number one health problem for women in industrialized countries. After menopause, the risk for women is almost equal to that of men.

Cardiovascular Disease Awareness

Cardiovascular diseases are called ”lifestyle diseases” because they are caused mostly by everyday choices that people make, such as what to eat for dinner, or what to do during their free time. For example, watching TV with your dog does not involve much moving around so it does not exercise the body, whereas bringing the dog for a walk outside exercises both of you. Decisions that you make today and everyday will affect your cardiovascular health many years from now, such as those shown in **Figure** 3.21.

Many studies have shown that plaque buildup starts in early adolescence. However, teens are more concerned about risks such as HIV, accidents, and cancer than cardiovascular disease. One in three people will die from complications due to atherosclerosis. For this reason there is an emphasis on the prevention of CVD through risk reduction. For example, healthy eating, regular physical activity, and avoidance of smoking can greatly decrease a person’s chance of developing a CVD.

Figure 3.21: Limiting sedentary activities such as watching TV, and making more time for walking, hiking, cycling, or running will help develop a healthy heart.

Congenital Heart Defects

A **congenital heart defect** is a problem with the structure of the heart that is present at birth. Such heart defects are the most common type of major birth defect. Most heart defects either obstruct blood flow in the heart or vessels near it, or cause blood to flow through the heart in an abnormal pattern, although other defects affecting heart rhythm can also occur.

Treatment for a defect can include medicines, surgery, and other medical procedures and heart transplants. The treatment depends on the type and severity of the defect and the child’s age, size and general health. Also, certain mild defects that some children are born with are repaired over time by the body.

Lesson Summary

- The main components of the cardiovascular system are the heart, the blood vessels, and the blood. It moves nutrients, hormones, gases and wastes to and from body cells, and distributes heat to maintain homeostasis.
- Deoxygenated blood enters the right atrium from the body through the vena cava; oxygenated blood coming from the lungs through the pulmonary vein enters the left atrium. The atria then contract, pushing the blood into the ventricles. After a short delay, the ventricles contract, the oxygenated blood gets pushed through the aorta to the rest of the body, and the deoxygenated blood gets pushed to the lungs through the pulmonary arteries.
- Arteries have thick walls that have three major layers; an inner endothelial layer, a middle layer of smooth muscle, and an outer layer of stretchy connective tissue (mostly collagen). The thick, outer layer of a vein is made up of collagen-containing connective tissue. The connective tissue is wrapped around bands of smooth muscle while the interior is lined with endothelium. Most veins have one-way flaps called valves that prevent blood from flowing backward and pooling in the legs, feet, arms or hands due to the pull of gravity. The walls of capillaries are made of only a single layer of endothelial cells.
- The lymphatic system has three related functions; the removal of excess fluids from body tissues, the absorption of fats and transport of fat to the cardiovascular system, and the production of certain types of white blood cells.
- Atherosclerosis, which may lead to a heart attack, is a chronic inflammatory response in the walls of arteries that leads to a buildup of plaque. Plaque is made of cell debris, cholesterol, fatty acids, calcium, and fibrous connective tissue that build up around an area of inflammation. As a plaque grows it stiffens and narrows the artery, which reduces the flow of blood through the artery.
- Eating nutritious food, being physically active for 60 minutes on most days of the week, and avoiding smoking are three of the most effective things a person can do to avoid cardiovascular disease.

Summary Animation

- http://www.hostos.cuny.edu/oaa/heart/heart.html

Review Questions

1. Why is the left ventricle generally thicker than the right ventricle?
2. At what point do the pulmonary and systemic circulation systems meet up?
3. Why do veins have valves? Use the heart **Figure** 3.22 to answer the following four questions:
4. What two structures are involved in the patent ductus arteriosus shown in this diagram. (Hint: The patent ductus arteriosus is the structure found inside the white circle at top center).
5. Propose what might happen to blood flow around the site of the PDA.
6. Would a PDA be considered a heart defect? Explain your answer.
7. How might the PDA affect the body? Use **Figure** 3.23 of the estimated prevalence of cardiovascular disease (CVD) in the U.S. population to answer the following three questions.
8. What is the overall trend in the prevalence of CVD in the U.S. population?
9. In what age group does the prevalence of CVD in the female population equal that of the male population?
10. At what point does 50 percent of the male and female population have CVD?

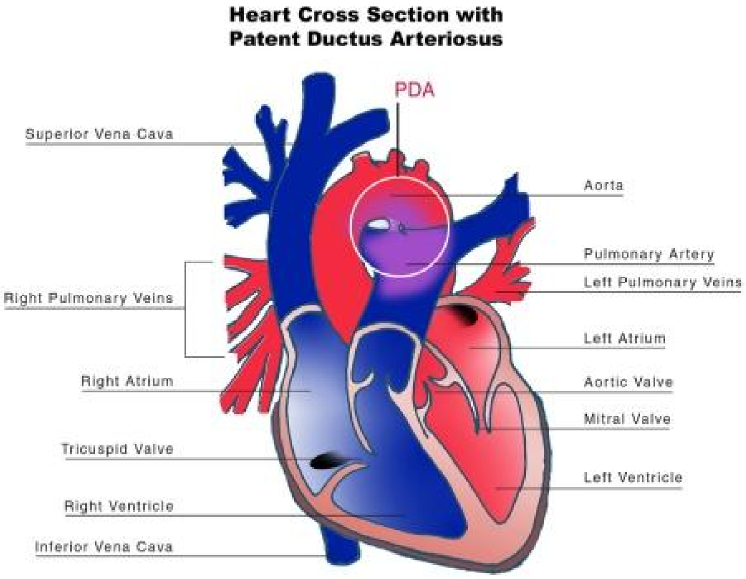

Figure 3.22

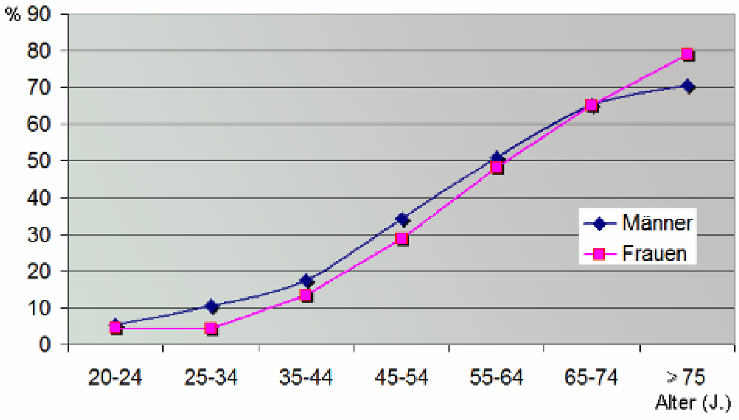

Figure 3.23

Further Reading / Supplemental Links

- Vanhecke et al. Awareness, knowledge, and perception of heart disease among adolescents. EJCPR 2006;13:718-723.
- Strong, J.P., et al. Prevalence and Extent of Atherosclerosis in Adolescents and Young Adults JAMA. 1999;281:727-735. Available online at:
- http://jama.ama-assn.org/cgi/content/full/281/8/727
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- http://www.nlm.nih.gov/medlineplus/ency/article/000171.htm#Causes,%20incidence,%20and%20risk%20facto
- http://www.nlm.nih.gov/medlineplus/congenitalheartdefects.html
- http://www.americanheart.org
- http://www.accessexcellence.org/
- http://whyfiles.org/090doping_sport/3.html
- http://whyfiles.org/
- http://en.wikipedia.org

Vocabulary

arteriole Small diameter blood vessel that extends and branches out from an artery and leads to capillaries.

artery Large, muscular vessels that carry blood away from the heart.

atria Thin-walled blood collection chambers of the heart, pump blood into the ventricles (singular, atrium).

atrioventricular node Conducts the electrical impulses that come from the SA node through the atria to the ventricles.

atrioventricular valves Ensure blood flows from the atria to the ventricles.

blood pressure The force exerted by circulating blood on the walls of blood vessels.

Bundle of His A collection of heart muscle cells (fibers) specialized for electrical conduction that transmits the electrical impulses from the AV node.

cardiovascular system An organ system that moves nutrients, hormones, gases and wastes to and from body cells, and distributes heat to maintain homeostasis.

capillary Smallest of the body's blood vessels, connects arterioles and venules, and are important for the interchange of gases and other substances between blood and body cells.

coronary circulation Supplies the heart tissue with blood.

diastole Period of time when the heart relaxes after contraction.

heart The muscular organ that pumps blood through the blood vessels by repeated, rhythmic contractions.

hypertension Condition in which a person's blood pressure is chronically high.

pulmonary circulation Portion of the cardiovascular system which carries deoxygenated blood away from the heart, to the lungs, and returns oxygenated blood back to the heart.

Purkinje fibers Specialized cardiac muscle cells that conduct action potentials into the ventricles, causing the cardiac muscle of the ventricles to contract in a controlled fashion.

semilunar valves Present in the arteries leaving the heart, prevent blood flowing back from the arteries into the ventricles.

sinoatrial node Known as the "cardiac pacemaker," found in the upper wall of the right atrium, is responsible for the wave of electrical stimulation that starts atrial contraction by creating an action potential.

sphygmomanometer Measures arterial pressure.

systemic circulation Portion of the cardiovascular system which carries oxygenated blood away from the heart, to the body, and returns deoxygenated blood back to the heart.

systole Contraction of the heart chambers, which drives blood out of the chambers.

vascular resistance Resistance to flow that blood must overcome to be pumped through your circulatory system.

vasoconstriction Constriction of blood vessels by contracting the vascular smooth muscle in the vessel walls.

vasodilatation Process by which blood vessels in the body become wider due to the relaxation of the smooth muscle in the vessel wall.

vein Vessel that carries blood toward the heart.

ventricles Heart chambers which collect blood from the atria and pump it out of the heart.

venule Small vessel that allows deoxygenated blood to return from the capillaries to veins.

Points to Consider

- How may factors such as the region of the world in which you live or your type of employment contribute to your risk of developing cardiovascular disease?
- Hypothesize about the role of blood in your excretory system.

3.3 Lesson 22.2: Blood

Lesson Objectives

- List three functions of blood.
- Describe the composition of blood.
- Outline the process of blood clotting.
- Identify two major blood group systems.
- Outline the significance of blood type in transfusions.
- Describe two diseases of the blood.

Introduction

Blood is a fluid connective tissue. It circulates around the body through the blood vessels by the pumping action of the heart. Arterial blood carries oxygen and nutrient to all the body's cells, and venous blood carries carbon dioxide and other metabolic wastes away from the cells.

In addition to the transport of gases, nutrients, and wastes, blood has many other functions that include:

- The removal of waste such as carbon dioxide, urea and lactic acid from the body tissues.
- The defense of the body against infection by microorganisms or parasites.
- The repair of damage to the body tissues.
- The transport of chemical messages, such as hormones and hormone-like substances.
- The control of body pH (the normal pH of blood is in the range of 7.35 - 7.45).
- The control of body temperature.

The Composition of Blood

Blood is a colloidal solution, it is made up of particles suspended in a fluid. It accounts for about 7% of the human body weight. The average adult has a blood volume of roughly 5 liters, composed of a fluid called plasma, and several kinds of cells. Within the blood plasma, are erythrocytes (red blood cells), leukocytes (white blood cells), thrombocytes (platelets) and other substances. The cells that make up the blood can be seen in **Figure** 3.24.

Plasma

Plasma is the golden-yellow liquid part of the blood. Plasma is 90% water and 10% dissolved materials including proteins, glucose, ions, hormones, and gases. It acts as a buffer, maintaining pH near 7.4. Plasma is about 54% the volume of blood; cells and fragments make up about 46% of the volume.

Red Blood Cells

Red blood cells, also known as **erythrocytes**, are flattened, doubly concave cells that carry oxygen. There are about 4 to 6 million cells per cubic millimeter of blood. Red blood cells make up about 45% of blood volume, as shown in **Figure** 3.25. Each red blood cell has 200 million hemoglobin molecules. Humans have a total of 25 trillion red blood cells (about 1/3 of all the cells in the body). Red blood cells are continuously made in the red marrow of long bones, ribs, skull, and vertebrae. Each red blood cell lives for only 120 days, after which they are destroyed in liver and spleen.

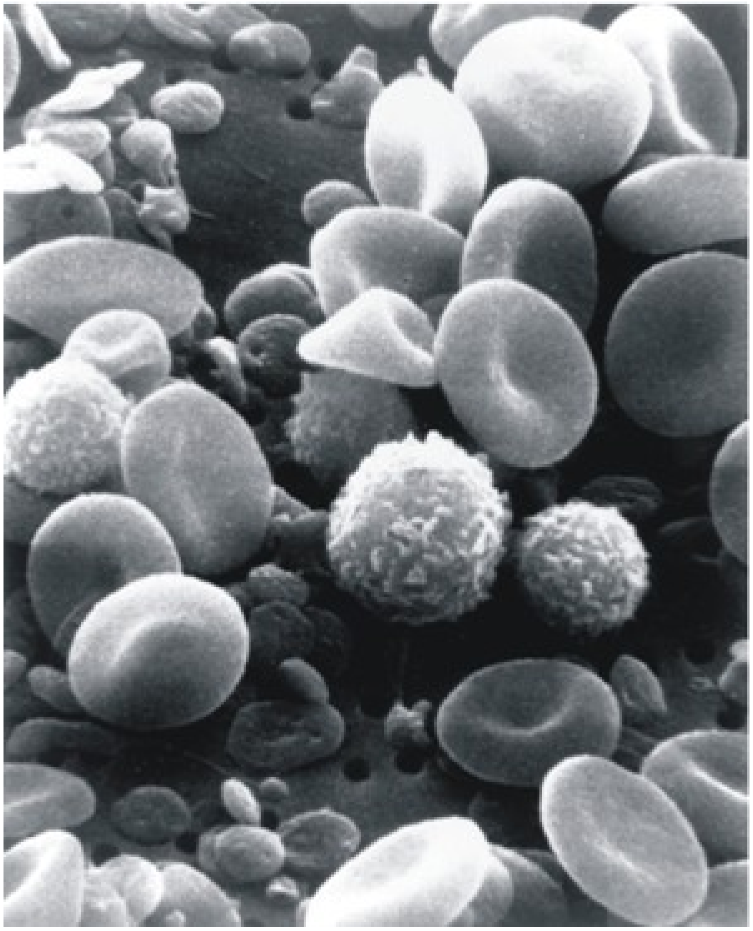


Figure 3.24: A scanning electron microscope (SEM) image of normal circulating human blood. One can see red blood cells, several white blood cells including knobby lymphocytes, a monocyte, a neutrophil, and many small disc-shaped platelets.

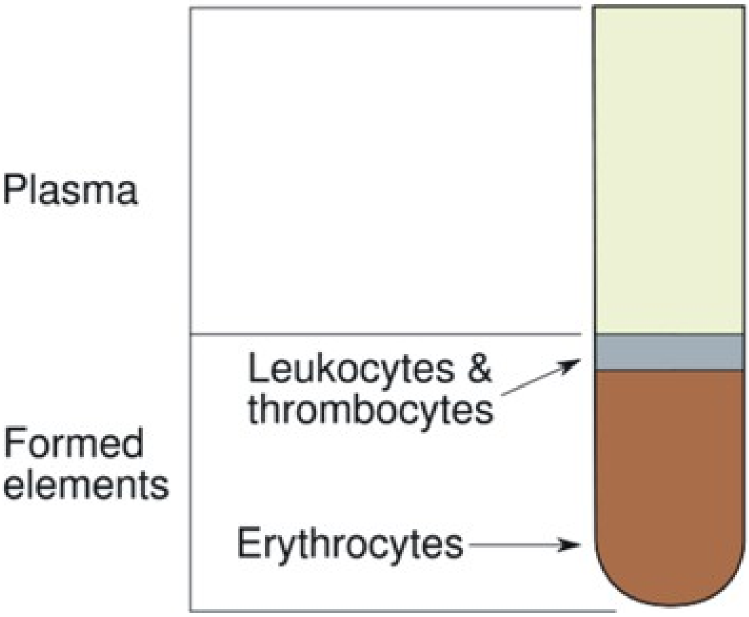


Figure 3.25: The components of blood. Red blood cells make up about 45% of the blood volume, white blood cells, about one percent, and platelets less than one percent. Plasma makes up the rest of the blood.

Mature red blood cells do not have a nucleus or other organelles. They contain the protein hemoglobin which gives blood its red color. The iron-containing heme portion of hemoglobin enables the protein to carry oxygen to cells. Heme binds to molecules of oxygen, which increases the ability of the blood to carry the gas.

Iron from hemoglobin is recovered and reused by red marrow. The liver degrades the heme units and secretes them as pigment in the bile, responsible for the color of feces. Each second two million red blood cells are produced to replace those thus taken out of circulation.

White Blood Cells

White blood cells, also known as **leukocytes**, are generally larger than red blood cells, as shown in **Figure** 3.26. They have a nucleus, but do not have hemoglobin. White blood cells make up less than one percent of the blood's volume. They are made from stem cells in bone marrow. They function in the cellular immune response. There are five types of white blood cells. Neutrophils enter the tissue fluid by squeezing through capillary walls and phagocytizing (swallowing) foreign bodies. Macrophages also swallow and destroy cell debris and bacteria or viruses. In **Figure** 3.27, a macrophage is shown phagocytizing two particles, possibly pathogens. Macrophages also release substances that cause the numbers of white blood cells to increase. Antigen-antibody complexes are swallowed by macrophages. Lymphocytes fight infection. T-cells attack cells containing viruses. B-cells produce antibodies. To learn more about the role of white blood cells in fighting infection, refer to the *Immune System and Disease* chapter.

Platelets

Platelets, also known as **thrombocytes**, are important in blood clotting. Platelets are cell fragments that bud off bone marrow cells called megakaryocytes. A platelet is shown in **Figure** 3.28. They make up less than one percent of blood volume. Platelets carry chemicals essential to blood clotting. They change fibrinogen into fibrin, a protein that creates a mesh onto which red blood cells collect, forming a clot. This

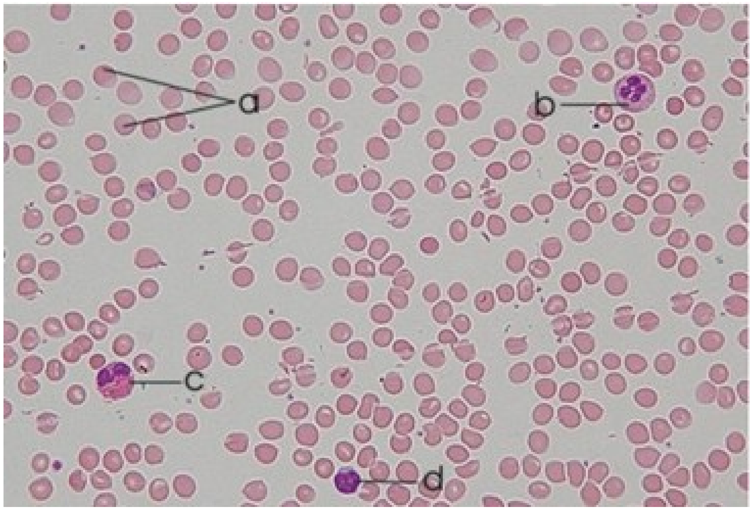


Figure 3.26: Relative sizes of red and white blood cells. a - red blood cells; b

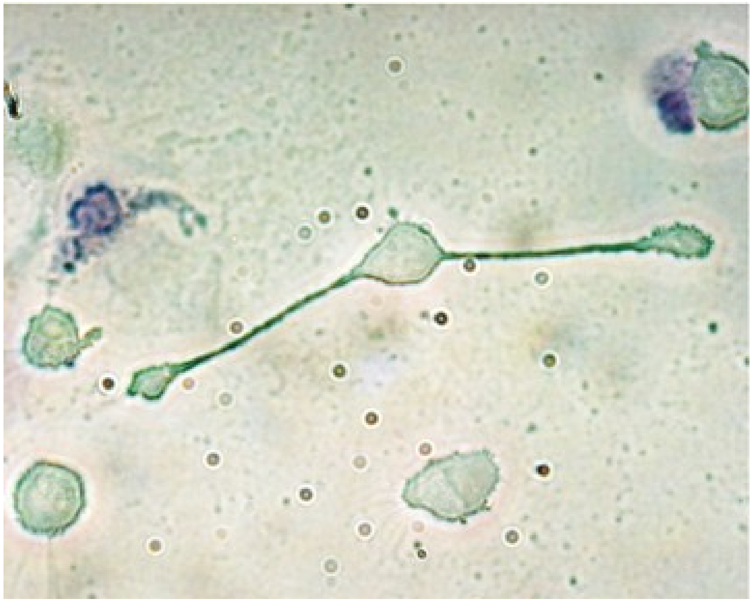


Figure 3.27: Macrophage showing cytoplasmic extensions that allow it to

clot stops more blood from leaving the body and also helps to prevent bacteria from entering the body. Platelets survive for 10 days before being removed by the liver and spleen. There are 150,000 to 300,000 platelets in each milliliter of blood. Platelets stick to tears in blood vessels and they release clotting factors.

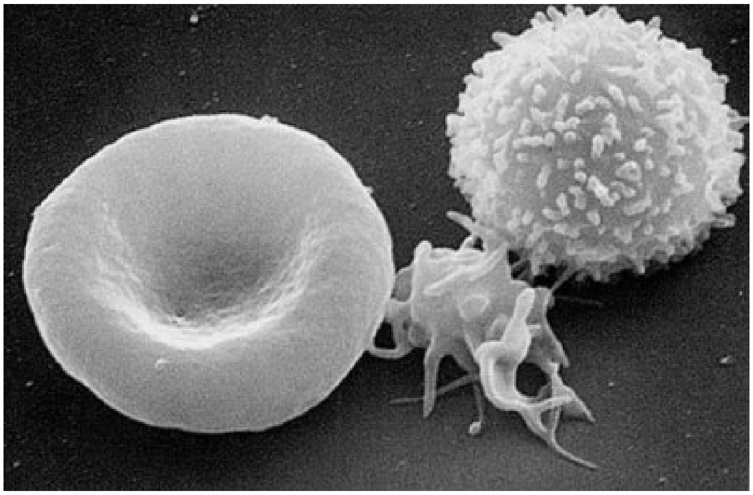


Figure 3.28: Cells of the blood. From left to right: Red blood cell, platelet, white blood cell. The concave side of red blood cells can be seen. Both sides of red blood cells are concave. The biconcave shape gives the red blood cells a smaller surface to volume ratio, which allows them to pick up large amounts of oxygen.

Other Blood Components

Blood plasma also contains other substances other than water. Some important components of blood include:

- Serum albumin: a plasma protein that acts as a transporter of hormones and other molecules.
- Antibodies: proteins that are used by the immune system to identify and destroy foreign objects such as bacteria and viruses.
- Hormones: chemical messengers that are produced by one cell and carried to another.
- Electrolytes such as sodium (Na+) and chloride (Cl-) ions.

Production and Breakdown of Blood Cells

Blood cells are produced in the red and yellow bone marrow in a process called **hematopoiesis**. Blood cells are broken down by the spleen and certain cells in the liver. The liver also clears some proteins, lipids and amino acids from the blood. The kidney actively secretes waste products of the blood into the urine.

Functions of Blood

Transport of Oxygen

The hemoglobin molecule is the major transporter of oxygen in mammals, including humans and many other species. About 98.5 percent of the oxygen in a sample of arterial blood in a healthy human is bonded with hemoglobin. Only 1.5 percent of the oxygen in blood is not carried by hemoglobin, instead it is dissolved in the plasma.

Under normal conditions in humans at rest, the hemoglobin in the red blood cells that are leaving the lungs is about 98 to 99 percent saturated with oxygen, and the blood is referred to as oxygenated. In a healthy adult at rest, deoxygenated blood returning to the lungs is still 75 percent saturated with oxygen. Oxygen saturation of arterial blood at or below 95 percent is considered dangerous in an individual at rest (for instance, during surgery under anesthesia)

Substances other than oxygen can bind to the hemoglobin; in some cases this can cause irreversible damage to the body. The gas carbon monoxide, for example, is very dangerous when absorbed into the blood. It bonds irreversibly with hemoglobin, which reduces the volume of oxygen that can be carried in the blood. Carbon monoxide poisoning can very quickly cause suffocation and death. Carbon monoxide is released during combustion (fire). It is released by cigarettes, barbeque grills, combustion of petrol products in cars and trucks, or anything else that can be burned.

Transport of Carbon Dioxide

When systemic arterial blood flows through capillaries, carbon dioxide diffuses from the tissues into the blood. Some carbon dioxide is dissolved in the blood. The remaining carbon dioxide is converted to bicarbonate and hydrogen ion which is then carried in the blood to the lungs, where it is converted back to carbon dioxide and released into the lungs.

Thermoregulation

Blood circulation transports heat through the body, and adjustments to this flow are an important part of thermoregulation. Increasing blood flow to the surface (e.g. during warm weather or strenuous exercise) causes warmer skin, resulting in greater heat loss. Decreasing surface blood flow conserves heat.

Blood Clotting

Coagulation, or **blood clotting**, is a complex process by which blood forms solid clots. Coagulation is important to stop bleeding and begin repair of damaged blood vessels. Blood clotting disorders can lead to an increased risk of bleeding or clotting inside a blood vessel. Platelets are important for the proper coagulation of blood.

Clotting is started almost immediately when an injury damages the endothelium of a blood vessel. Platelets clump together, forming a plug at the site of injury. Then, proteins in the plasma called **coagulation factors**, respond in a series of chemical reactions that form a tough protein called **fibrin**. The fibrin strands form a web across the platelet plug, trapping red blood cells before they can leave through the wound site. This mass of platelets, fibrin, and red blood cells forms a clot that hardens into a scab.

Certain nutrients are needed for the proper functioning of the clotting mechanism. Two of these are calcium and vitamin K. Luckily for you, bacteria that live in your intestines make enough vitamin K so you do not need to have extra in your food.

Blood Types

Blood type (also called a **blood group**), is determined by the presence or absence of certain molecules, called antigens, on the surface of red blood cells. An **antigen** is a molecule or substance that causes an immune response. Blood type antigens may be proteins, or carbohydrates, depending on the blood group system. The antigens on a person's own body cells are recognized by their immune system as "self" antigens, and their immune system does not attack them. However, if a person is exposed to a blood group antigen that is different from their own blood group, the person's immune system will produce antibodies against the donor blood antigens. These antibodies can bind to antigens on the surface of transfused red blood cells (or other tissue cells) often leading to destruction of the cells by the immune system.

The erythrocyte surface antigens that have one allele, or a group of very closely linked genes, are collectively called a ”blood group system”. There are 29 known blood group systems in humans, but the ABO blood group system and the Rhesus (Rh) blood group system are the most important for blood transfusions.

ABO Blood Group System

In 1875, a German physiologist, Leonard Landois reported that the blood cells of a human and an animal would clump together when mixed. In the early 1900s, Austrian biologist and physician Karl Landsteiner pointed out that a similar clumping reaction occurred when the blood of one person was transfused with another. He determined that this might be the cause of shock, jaundice, and release of hemoglobin that had followed some earlier attempts at person-to-person blood transfusions.

In 1909, Landsteiner classified blood into the A, B, AB, and O groups. He also showed that transfusions between of the same blood group did not result in the destruction of blood cells and that clumping occurred only when a person was transfused with the blood of a person belonging to a different blood group.

The ”A” and ”B” of the ABO blood group refer to two carbohydrate antigens found on the surface of red blood cells. There is not an O antigen. Type O red blood cells do not have either type A or B antigens on their surface, as listed in **Table** 3.1. Antibodies are found in the blood plasma. The blood type of a person can be determined by using antibodies that bind to the A or B antigens of red blood cells.

Table 3.1: **Blood Types, Antigen Types, and Antibody Types**

Blood Type	Antigen Type	Serum (Plasma) Antibodies	Can Receive Blood from Types	Can Donate Blood to Types
A	A	anti-B	A, O	A, AB
B	B	anti-A	B, O	B, AB
AB	A and B	none	AB, A, B, O	AB
O	none	anti-A, anti-B	O	AB, A, B, O

(*Source:* CK12 Foundation, *License:* CC-BY-SA)

Agglutination is the clumping of red blood cells that occurs when different blood types are mixed together, shown in **Figure** 3.29. It involves a reaction between antigens on the surface of red blood cells and protein antibodies in the blood plasma. Mixing different blood types together can cause agglutination, a process that has been used as a way of determining a person's blood type.

Rhesus Blood Group System

The **Rhesus system** is the second most significant blood group system in human blood transfusion. The most significant Rhesus antigen is called the **RhD antigen**, also called Rhesus factor. A person either has, or does not have the RhD antigen on the surface of their red blood cells. This is usually indicated by ”RhD positive” (does have the RhD antigen) or ”RhD negative” (does not have the antigen) suffix to the ABO blood group (see blood agglutination test in **Figure** 3.30).

The Rhesus system is named after the Rhesus monkey, in which the antigen was first discovered by Karl

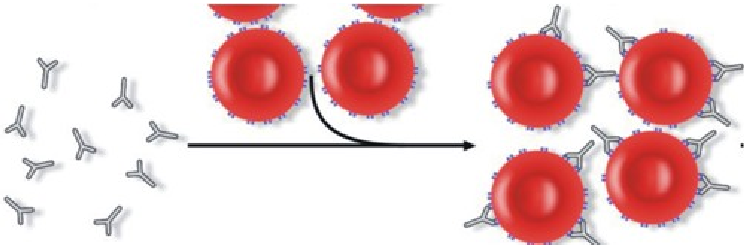


Figure 3.29: Antigens on the red blood cell surface. Antibodies attach to the antigens on the red blood cell, causing the blood cells to clump together. This leads to agglutination of the blood.

Landsteiner and Alexander S. Wiener in 1937. The importance of the Rh factor was realized soon after. Dr. Phillip Levine, a pathologist who worked at a New York hospital, made the connection between the Rh factor and the incidence of a blood disease in newborn babies. The disease, called hemolytic disease of the newborn is a condition that develops while the fetus is in the womb. If a mother is RhD negative, and the father is RhD positive, the fetus may inherit the dominant RhD positive trait from the father. The RhD negative mother can make antibodies against the RhD antigens of her developing baby. This can happen if some of the fetus' blood cells pass into the mother's blood circulation, or if the mother has received an RhD positive blood transfusion.

The fetus' red cells are broken down and the fetus can develop anemia. This disease ranges from mild to very severe, and fetal death from heart failure can occur. Most RhD disease can be prevented by treating the mother during pregnancy or soon after childbirth. The mother is injected with anti-RhD antibodies, so that the baby's red blood cells are destroyed before her body can produce antibodies against them. If a pregnant woman is known to have anti-RhD antibodies, the RhD blood type of a fetus can be tested by analysis of fetal DNA in maternal plasma to assess the risk to the fetus of Rh disease.

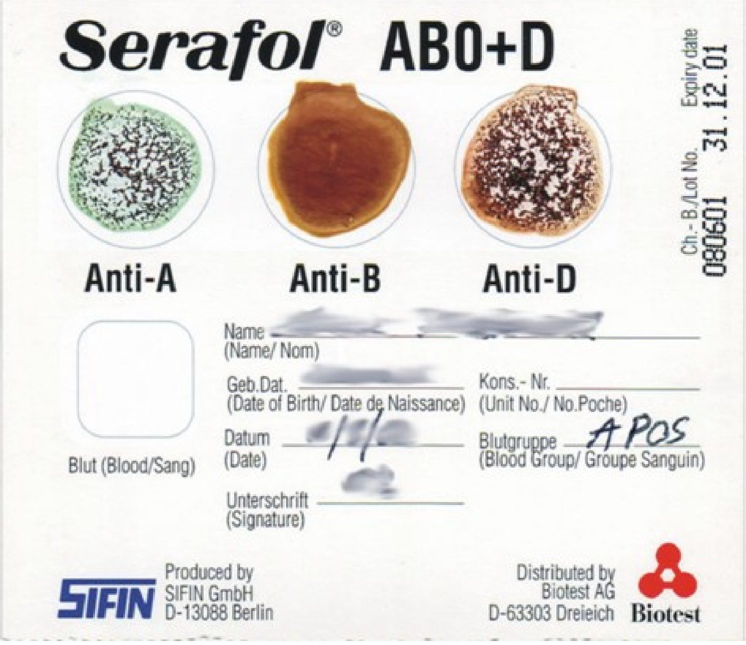
The presence or absence of the ABO group antigens and the RhD antigens are always determined for all recipient and donor blood. **Figure** 3.30 shows a routine way in which a person's ABO blood group is determined.

Blood Products

In order to provide maximum benefit from each blood donation and to extend shelf-life, blood banks separate some whole blood into several different products. Some of the most common of these products are packed red blood cells, plasma, platelets, and fresh frozen plasma. Units of packed red blood cells are made by removing as much of the plasma as possible from whole blood units. Clotting factors made by genetic engineering are now routinely used for the treatment of the clotting disorder hemophilia, so the risk of possible infection from donated blood products is avoided.

Universal Donors and Universal Recipients

Regarding the donation of packed red blood cells, individuals with type O negative blood are often called **universal donors**, and those with type AB positive blood are called **universal recipients**. Type O red blood cells do not have the A or B antigens, and can be given to people with a different ABO blood group. The blood plasma of an AB person does not contain any anti-A or anti-B antibodies, so they can receive any ABO blood type. The possible reactions of anti-A and anti-B antibodies in the donor blood to the recipient's red blood cells are usually not a problem because only a small volume of plasma that containing antibodies is given to the recipient. Refer to **Table** 3.1 for a complete listing of ABO antigens and antibodies that are involved in the ABO system.



Serafol® ABO+D

Ch.-B./Lot No. 080601
Expiry date 31.12.01

Anti-A Anti-B Anti-D

Name (Name/ Nom) [redacted]
Geb.Dat. (Date of Birth/ Date de Naissance) [redacted]
Kons.-Nr. (Unit No./ No.Poche)
Datum (Date) [redacted]
Blutgruppe (Blood Group/ Groupe Sanguin) A POS
Unterschrift (Signature) [redacted]
Blut (Blood/Sang)

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Figure 3.30: A bedside blood grouping card showing the agglutination of the blood with anti-A and anti-Rh(D), but not with anti-B. Therefore the blood group is A positive. This method of blood grouping relies on seeing an agglutination reaction to determine a person

In April 2007 researchers discovered a way to convert blood types A, B, and AB to O; the method used enzymes that removed the antigens on the surface of the red blood cells.

Other Blood Group Systems

You probably have heard a lot about the ABO and Rhesus (RhD) blood group systems by now, but you have probably not heard much about the other 27 other systems. Many other antigens are found on the cell membrane of red blood cells. For example, an individual can be AB RhD positive, and at the same time M and N positive (MNS system), K positive (Kell system), Le^a or Le^b negative (Lewis system), Duffy positive, or Duffy negative (Duffy system), and so on, being positive or negative for each blood group system antigen. Many of the blood group systems were named after the patients in whom the antibodies were first found.

Some blood group systems are associated with a disease, for example, the Kell antigen is associated with McLeod syndrome, a genetic disorder in which the red blood cells are spiky shaped. Certain other blood group systems may affect resistance to infections, an example being the resistance to specific malaria species seen in individuals who lack the Duffy antigen. The Duffy antigen is less common in ethnic groups from areas with a high incidence of malaria.

Rare blood types can cause supply problems for blood banks and hospitals. For example Duffy-negative blood occurs much more frequently in people of African origin, and the rarity of this blood type in the rest of the population can result in a shortage of Duffy-negative blood. Similarly, for RhD negative people, there is a risk associated with traveling to parts of the world where supplies of RhD negative blood are rare, particularly East Asia.

Homeostatic Imbalances of the Blood

Problems can occur with red blood cells, white blood cells, platelets, and other components of the blood. Many blood disorders are genetic, they are inherited from a parent, some are a result of nutrient deficiency, while others are cancers of the blood.

Sickle-cell disease is a group of genetic disorders caused by abnormally shaped hemoglobin, called sickle hemoglobin. In many forms of the disease, the red blood cells change shape because the abnormal hemoglobin proteins stick to each other, causing the cell to get a rigid surface and sickle shape, shown in **Figure** 3.31. This process damages the membrane of the red blood cell, and can cause the cells to get stuck in blood vessels. This clotting causes oxygen starvation in tissues, which may cause organ damage such as stroke or heart attack. The disease is chronic and lifelong. Individuals are most often well, but their lives are punctuated by periodic painful attacks. Sickle-cell disease occurs more commonly in people (or their descendants) from parts of the world such as sub-Saharan Africa, where malaria is or was common. It also occurs in people of other ethnicities. As a result, those with sickle cell disease are resistant to malaria since the red blood cells are not favored by the malaria parasites. The mutated hemoglobin allele is recessive, meaning it must be inherited from each parent for the individual to have the disease.

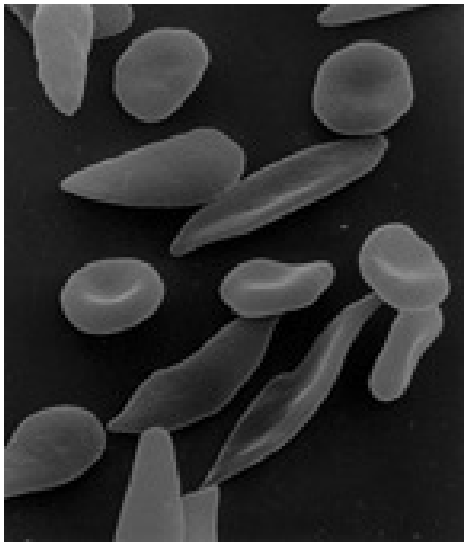

Figure 3.31: Sickle-cell disease. The abnormal shape of the red blood cells damages the red blood cells which causes them to get stuck in blood vessels. The blocked capillaries reduce the blood flow to an organ, and can result in pain and organ damage.

Iron deficiency anemia is the most common type of anemia. It occurs when the dietary intake or absorption of iron is less than what is needed by the body. As a result, hemoglobin, which contains iron, cannot be made. In the United States, 20 percent of all women of childbearing age have iron deficiency anemia, compared with only 2 percent of adult men. The principal cause of iron deficiency anemia in premenopausal women is blood lost during menstruation.

Leukemia is a cancer that originates in the bone marrow and is characterized by an abnormal production of white blood cells (rarely red blood cells) that are released into the bloodstream. **Lymphoma** is a cancer of the lymphatic system, which helps to filter blood. Lymphoma can be categorized as either Hodgkin's lymphoma or non-Hodgkin's lymphoma.

Hemophilia is the name of a group of hereditary genetic diseases that affect the body's ability to control blood clotting. Hemophilia is characterized by a lack of clotting factors in the blood. Clotting factors are needed for a normal clotting process. When a blood vessel is injured, a temporary scab does form, but the missing coagulation factors prevent the formation of fibrin which is needed to maintain the blood clot. Therefore, a person who has hemophilia is initially able to make a clot to stop the bleeding, but because fibrin is not produced, the body is unable to maintain a clot for long. The risks of the re-bleeding of an injury and internal bleeding are increased in hemophilia, especially into muscles, joints, or bleeding into closed spaces.

Haemochromatosis is a hereditary disease that is characterized by a buildup of iron in the body. Iron accumulation can eventually cause end organ damage, most importantly in the liver and pancreas, manifesting as liver failure and diabetes mellitus respectively. It is estimated that roughly one in every 300-400 people is affected by the disease, primarily of Northern European and especially people of Irish, Scottish, Welsh and English descent.

Lesson Summary

- The functions of blood include the removal of wastes such as carbon dioxide, urea and lactic acid from the body tissues; defense of the body against infection by microorganisms or parasites; repair of damage to the body tissues; transport of chemical messages, such as hormones and hormone-like substances; control of body pH; control of body temperature.
- Within the blood plasma are the red blood cells, white blood cells, platelets, and other substances. Red blood cells are the most common types of cells in the blood, they make up about 45 percent of blood volume.
- Blood clotting begins when the endothelium of a blood vessel is torn. Platelets clump together, forming a plug at the site of injury. Then, the coagulation factors cause a series of chemical reactions that form fibrin. The fibrin strands form a web across the platelet plug, trapping red blood cells before they can leave through the wound site. This mass of platelets, fibrin, and red blood cells forms a clot that hardens into a scab.
- There are 29 blood group systems, but the two major ones are the ABO and Rhesus systems.
- The ABO system is of great importance in blood transfusions. Individuals with type O negative blood are called universal donors, and those with type AB positive blood are called universal recipients. Type O red blood cells do not have the A or B antigens, and can be given to people with a different ABO blood group. The blood plasma of an AB person does not contain any anti-A or anti-B antibodies, so they can receive any ABO blood type.
- Iron deficiency anemia is the most common type of anemia. It occurs when the dietary intake or absorption of iron is less than what is needed by the body. As a result, hemoglobin, which contains iron, cannot be made. Hemophilia is the name of a group of hereditary genetic diseases that affect the body's ability to control blood clotting. Hemophilia is characterized by a lack of clotting factors in the blood.

Review Questions

1. Name the four main components of blood.
2. How does the structure of a red blood cell relate to its function?
3. Name one other gas that can bind to hemoglobin, and identify an affect that such binding can have on homeostasis.
4. Why might iron-deficiency anemia cause a person to feel tired?
5. Identify two different types of human blood systems.
6. Identify the processes involved in blood clotting.
7. A sample of blood taken from a patient has elevated (higher than normal) levels of leucocytes. What could this mean?

8. Identify where in the body red blood cells and white blood cells are made.
9. Explain why taking erythropoietin (EPO), which stimulates the production of more red blood cells, is considered a form of cheating in sports.

Further Reading / Supplemental Links

- http://www.estrellamountain.edu/faculty/farabee/biobk
- http://waynesword.palomar.edu/aniblood.htm
- http://en.wikipedia.org

Vocabulary

agglutination The clumping of red blood cells that occurs when different blood types are mixed together.

antibodies Proteins that are used by the immune system to identify and destroy foreign objects such as bacteria and viruses.

blood A fluid connective tissue; arterial blood carries oxygen and nutrient to all the body's cells, and venous blood carries carbon dioxide and other metabolic wastes away from the cells.

blood type (blood group) Determined by the presence or absence of certain molecules, called antigens, on the surface of red blood cells.

coagulation Blood clotting, a complex process by which blood forms solid clots.

coagulation factors Proteins in the plasma which respond damage to a blood vessel; response includes a series of chemical reactions that form a tough protein called fibrin.

erythrocytes Red blood cells; flattened, doubly concave cells that carry oxygen.

haemochromatosis A hereditary disease that is characterized by a buildup of iron in the body; can eventually cause end organ damage, most importantly in the liver and pancreas, manifesting as liver failure and diabetes mellitus respectively.

hematopoiesis The production of blood cells in the red and yellow bone marrow.

heme The iron-containing portion of hemoglobin; enables the protein to carry oxygen to cells.

hemoglobin Protein in red blood cells that carries oxygen.

hemophilia The name of a group of hereditary genetic diseases that affect the body's ability to control blood clotting.

hormones Chemical messengers that are produced by one cell and carried to another.

leukemia A cancer that originates in the bone marrow and is characterized by an abnormal production of white blood cells.

leukocytes White blood cells; function in the cellular immune response; includes neutrophils, eosinophils, and macrophages.

lymphoma A cancer of the lymphatic system, which helps to filter blood; can be categorized as either Hodgkin's lymphoma or non-Hodgkin's lymphoma.

plasma The golden-yellow liquid part of the blood; 90% water and 10% dissolved materials including proteins, glucose, ions, hormones, and gases.

serum albumin A plasma protein that acts as a transporter of hormones and other molecules.

sickle-cell disease A group of genetic disorders caused by abnormally shaped hemoglobin, called sickle hemoglobin.

thrombocytes Platelets; important in blood clotting; cell fragments that bud off bone marrow cells called megakaryocytes.

universal donors Individuals with type O negative blood.

universal recipients Individuals with type AB positive blood.

Points to Consider

- How might the composition of your blood change during a 24-hour period?
- What do you think is the relationship between the cardiovascular system, blood, and the respiratory system?

3.4 Respiratory System

Lesson Objectives

- Distinguish between external and internal respiration.
- Identify the structures of the respiratory system.
- Outline the process of inhalation.
- Describe how carbon dioxide is carried in the blood.
- Compare the causes of emphysema and asthma.

Introduction

Have you ever wondered what it would be like to have gills? You would breathe and look very different from the rest of us, but they would be great for swimming and diving! Despite such differences, the main functions of lungs and gills are the same: to obtain oxygen, and to release carbon dioxide.

The human respiratory system brings oxygen, O_2, into the body and releases carbon dioxide, CO_2, into the atmosphere. Oxygen is drawn in through the respiratory tract, which is shown in **Figure** 3.32, and is then delivered to the blood. This process is called **external respiration**. The exchange of gases between the blood and the cells of the body is called **internal respiration**.

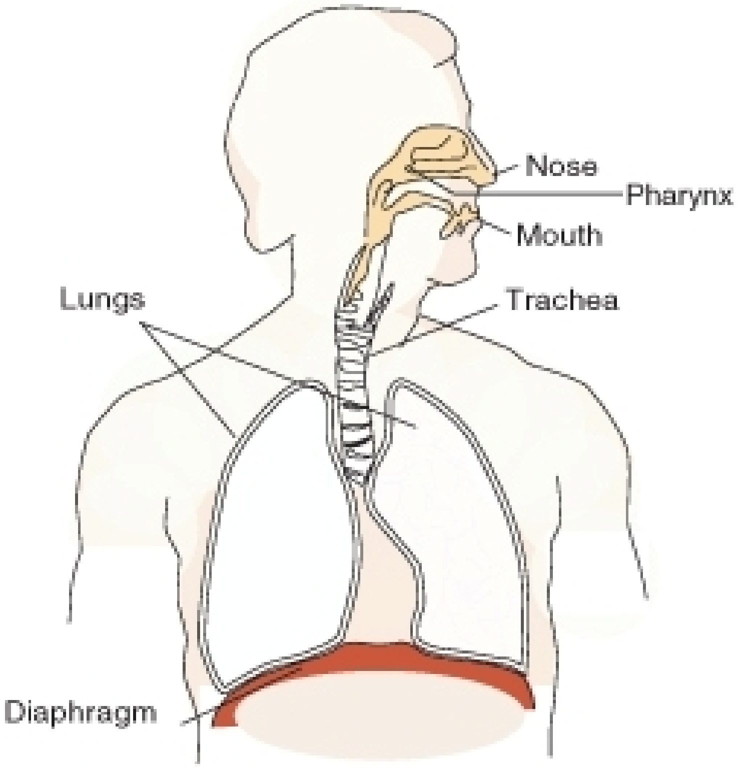

Figure 3.32: The respiratory system. Air moves down the trachea, a long straight tube in the chest. The diaphragm pulls air in and pushes it out. Respiratory systems of various types are found in a wide variety of organisms.

Comparing ”Cellular Respiration” and ”Respiration”

Respiration is the transport of oxygen from the outside air to the cells of the body, and the transport of carbon dioxide in the opposite direction. This is in contrast to the biochemical definition of respiration, which refers to cellular respiration. **Cellular respiration** is the metabolic process by which an organism obtains energy by reacting oxygen with glucose to give water, carbon dioxide and ATP (energy). Although respiration is necessary to sustain cellular respiration and thus life in animals, the processes are very different. Cellular respiration takes place in individual cells of the animal, while respiration involves the transport of metabolites between the organism and external environment.

Structures of the Respiratory System

The nose and **nasal cavity** filter, warm, and moisten the inhaled air. The nose hairs and mucus produced by the epithelial cells in the nose catch airborne particles and prevent them from reaching the lungs.

Behind the nasal cavity, air next passes through the **pharynx**, a long tube that is shared with the digestive system. Both food and air pass through the pharynx. A flap of connective tissue called the **epiglottis** closes over the trachea when food is swallowed to prevent choking or inhaling food. In humans the pharynx is important in vocalization

The **larynx**, also called the voicebox, is found just below the point at which the pharynx splits into the trachea and the esophagus, shown in **Figure** 3.33. The voice is generated in the larynx. Air from the lungs is needed for the vocal folds to produce speech.

The **trachea**, or wind pipe, is a long tube that leads down to the chest where it divides into the right and left **bronchi** in the lungs. The bronchi branch out into smaller bronchioles, which are the first airway passages that do not contain cartilage. The bronchioles lead into the **alveoli**, which are the multi-lobed sacs in which most of the gas exchange occurs.

The Journey of a Breath of Air

In air-breathing vertebrates such as humans, respiration of oxygen includes four stages:

1. Ventilation from the atmosphere into the alveoli of the lungs.
2. Pulmonary gas exchange from the alveoli into the pulmonary capillaries.
3. Gas transport from the pulmonary capillaries through the circulation to the peripheral capillaries in the organs.
4. Peripheral gas exchange from the tissue capillaries into the cells and mitochondria.

Ventilation: From the Air to the Alveoli

Air enters the body through the nose, is warmed, filtered, and passed through the nasal cavity. Air passes the pharynx (which has the epiglottis that prevents food from entering the trachea). The upper part of the trachea contains the larynx. The vocal cords are two bands of tissue that extend across the opening of the larynx. After passing the larynx, the air moves into the trachea. The trachea is a long tube that divides into two smaller tubes called bronchi which lead into each lung, shown in **Figure** 3.33. Bronchi are reinforced to prevent their collapse and are lined with ciliated epithelium and mucus-producing cells. Bronchi branch into smaller and smaller tubes called bronchioles. Bronchioles end in grape-like clusters called alveoli. Alveoli are surrounded by a network of thin-walled capillaries, shown in **Figure** 3.34.

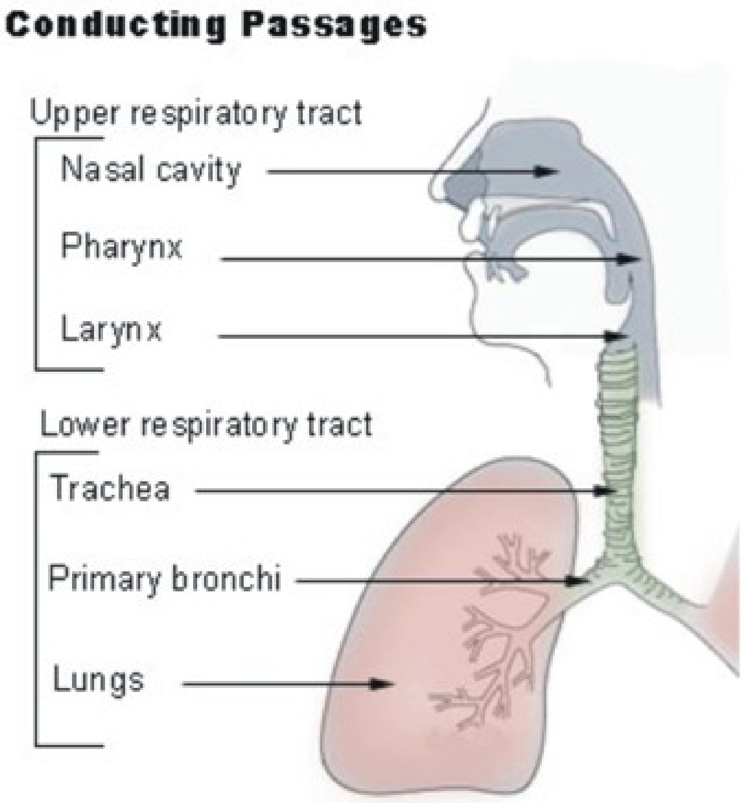

Figure 3.33: The structures of the respiratory system include the nasal cavity, the pharynx, larynx, which together are the upper respiratory tract. The trachea, bronchi, bronchioles and alveoli are part of up the lower respiratory tract.

Breathing in, or inhaling, is usually an active movement, contraction of the diaphragm muscles uses ATP. The **diaphragm** is a muscle that is found below the lungs (shown in **Figure** 3.32). Contraction of the diaphragm causes the volume of the chest cavity to increase, and the air pressure within the lungs to decrease. The pressure difference causes air to rush into the lungs. Relaxation of the diaphragm causes the lungs to recoil and air is pushed out of the lungs. Breathing out, or exhaling, is normally a passive process powered by the elastic recoil of the chest, similar to letting the air out of a balloon.

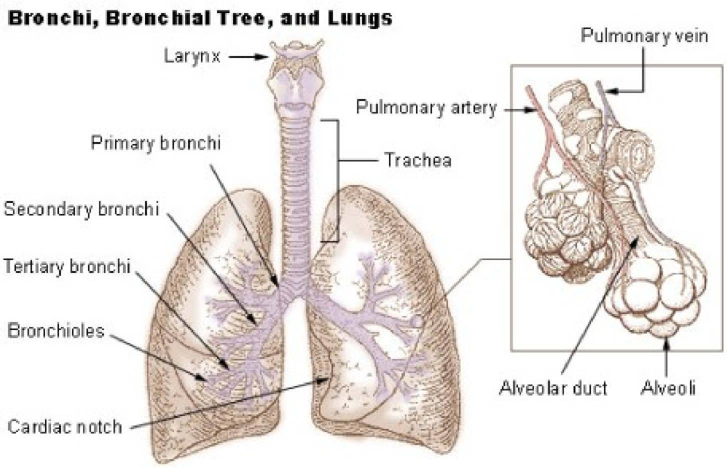

Figure 3.34: The alveoli are the tiny grape-like structures within the lungs, and are the site of pulmonary gas exchange.

Pulmonary Gas Exchange: From the Alveoli into the Pulmonary Capillaries

Breathing is only part of the process of delivering oxygen to where it is needed in the body. The process of **gas exchange** occurs in the alveoli by diffusion of gases between the alveoli and the blood passing in the lung capillaries, as shown in **Figure** 3.35. Recall that diffusion is the movement of substances from an area of higher concentration to an area of lower concentration. The difference between the high concentration of O_2 in the alveoli and the low O_2 concentration of the blood in the capillaries is enough to cause O_2 molecules to diffuse across the thin walls of the alveoli and capillaries and into the blood. CO_2 moves out of the blood and into the alveoli in a similar way. The greater the concentration difference, the greater the rate of diffusion.

Breathing also results in loss of water from the body. Exhaled air has a relative humidity of 100 percent because of the diffusion of water that from the moist surface of the breathing passages and the alveoli into the warm exhaled air.

In the lungs, oxygen is transported across the thin membranes of the alveoli and the border of the capillary and attracted to the hemoglobin molecule within the red blood cell.

After leaving the lungs, the oxygenated blood returns to the heart to be pumped through the aorta and around the body. The oxygenated blood travels through the aorta, to the smaller arteries, arterioles, and finally to the peripheral capillaries where gas exchange occurs.

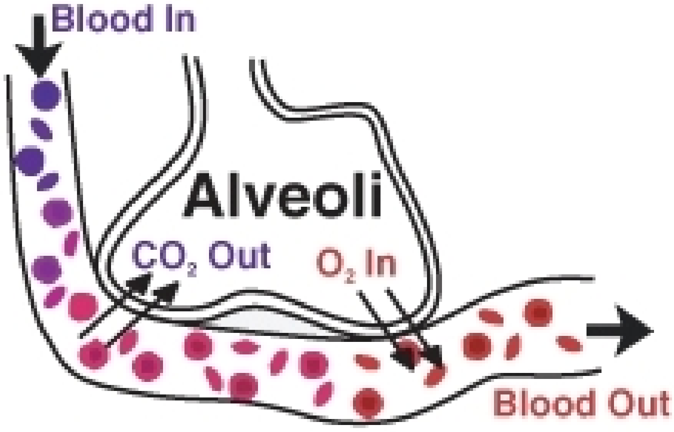

Figure 3.35: Gas exchange happens in the lungs through diffusion. Deoxygenated blood has a high concentration of CO

Peripheral Gas Exchange: From Capillaries into Cells, and from Cells into Capillaries

The oxygen concentration in body cells is low, while the blood that leaves the lungs is 97 percent saturated with oxygen. So, oxygen diffuses from the blood into the body cells when it reaches the peripheral capillaries (the capillaries in the systemic circulation).

Carbon dioxide concentration in metabolically active cells is much greater than in capillaries, so carbon dioxide diffuses from the cells into the capillaries. Most of the carbon dioxide (about 70 percent) in the blood is in the form of bicarbonate (HCO_3^-). A small amount of carbon dioxide dissolves in the water in the plasma to form carbonic acid (H_2CO_3). Carbonic acid and bicarbonate play an important role in regulating the pH of the body.

In order to remove CO_2 from the body, the bicarbonate is picked up by a red blood cell, and is again turned in to carbonic acid. A water molecule (H_2O) is then taken away from the carbonic acid, and the remaining CO_2 molecule is expelled from the red blood cells and into the alveoli where it is exhaled. The following equation shows this process:

$HCO_3^- + H^+ \quad H_2CO_3 \quad CO_2 + H_2O$

Gas exchange between your body and the environment occurs in the alveoli. The alveoli are lined with pulmonary capillaries, the walls of which are thin enough to permit the diffusion of gases. Inhaled oxygen diffuses into the pulmonary capillaries, where it binds to hemoglobin in the blood. Carbon dioxide diffuses in the opposite direction, from capillary blood to alveolar air. At this point, the pulmonary blood is oxygen-rich, and the lungs are primarily holding carbon dioxide. Exhalation follows, thereby ridding the body of the carbon dioxide and completing the cycle of respiration.

Gas Exchange and Homeostasis

The equilibrium between carbon dioxide and carbonic acid is very important for controlling the acidity of body fluids. As gas exchange occurs, the pH balance of the body is maintained as part of homeostasis. If proper respiration is interrupted two things can occur:

1. Respiratory acidosis, in which arterial blood contains too much carbon dioxide, causing a drop in

blood pH.

2. Respiratory alkalosis results from increased respiration (or hyperventilation) which causes a drop in the amount of carbon dioxide in the blood plasma. The drop in carbon dioxide concentration causes the blood pH to rise.

Control of Breathing by the Nervous System

Breathing is one of the few bodily functions which, within limits, can be controlled both consciously and unconsciously. Conscious attention to breathing is common in activities such as yoga, swimming, and karate. In speech or vocal training, a person learns to discipline his or her breathing for purposes other than life support.

Muscular contraction and relaxation controls the rate of expansion and constriction of the lungs. These muscles are controlled by the autonomic nervous system from the parts of the brainstem that control breathing: the medulla and the pons. This area of the brainstem forms the respiration regulatory center. When carbon dioxide levels increase in the blood (in the form of carbonic acid), such as during exercise, the pH level of the blood drops. This causes the medulla to send nerve impulses to the diaphragm and the muscles between the ribs, causing them to contract and increase the rate of breathing. This automatic control of respiration can be impaired in premature babies, or by drugs or disease.

Without breathing, the body's oxygen levels drop dangerously low within minutes, leading to permanent brain damage followed by death. It is not possible for a healthy person to voluntarily stop breathing indefinitely. If we do not inhale, the level of carbon dioxide builds up in our blood and we experience great air hunger. Eventually, not breathing leads to a loss of consciousness at which time the autonomic nervous system takes control and initiates breathing.

Inhalation

Inhalation is started by the diaphragm and supported by the external intercostal muscles (the muscles that are between the ribs). It is an active process that needs ATP. When the diaphragm contracts, the ribcage expands and the contents of the abdomen are moved downward. This results in a larger thoracic (chest) volume, which in turn causes a decrease in air pressure inside the lungs. As the pressure in the chest falls, air from outside the body moves into the respiratory system. Normal resting respirations are 10 to 18 breaths per minute. During an average breath, an adult will exchange from 500 ml to 700 ml of air. The average breath capacity of a person is called **lung volume**, or tidal volume.

Exhalation

Exhalation is generally a passive process, however active, or forced, exhalation is carried out by the abdominal and the internal intercostal muscles. The lungs have a natural elasticity and as they recoil from the stretch of inhalation, air flows out of the lungs until the pressures in the chest and the atmosphere reach equilibrium. During forced exhalation, as when blowing out a candle, expiratory muscles including the abdominal muscles and internal intercostal muscles generate pressure in the chest and abdomen, which forces air out of the lungs.

Homeostatic Imbalances of the Respiratory System: Diseases and Disorders

Respiratory disease is the term for diseases of the lung, bronchial tubes, trachea and throat. These diseases range from mild, such as a cold, to being possibly life-threatening, such as bacterial pneumonia.

Respiratory diseases can be grouped as either obstructive (conditions which lower the rate of the airflow into and out of the lungs, such as in asthma) or restrictive (conditions that cause a reduction in the functional volume of the lungs, such as emphysema.)

Emphysema is a chronic lung disease caused by loss of elasticity of the lung tissue. The destruction of elastic structures that support the alveoli and the capillaries that feed the alveoli cause them to become hard and stiff. Eventually the walls of the alveoli break down and the alveoli become larger. The amount of oxygen that can enter the blood with each breath is reduced because the large alveoli cannot function efficiently; much of the oxygen that gets into the large alveoli cannot be absorbed into the blood so the oxygen is unused. Symptoms include shortness of breath on exertion (usually when climbing stairs or a hill, and later at rest), and an expanded chest. Damage to the alveoli, which can be seen in **Figure** 3.36, is irreversible. Smoking is a leading cause of emphysema.

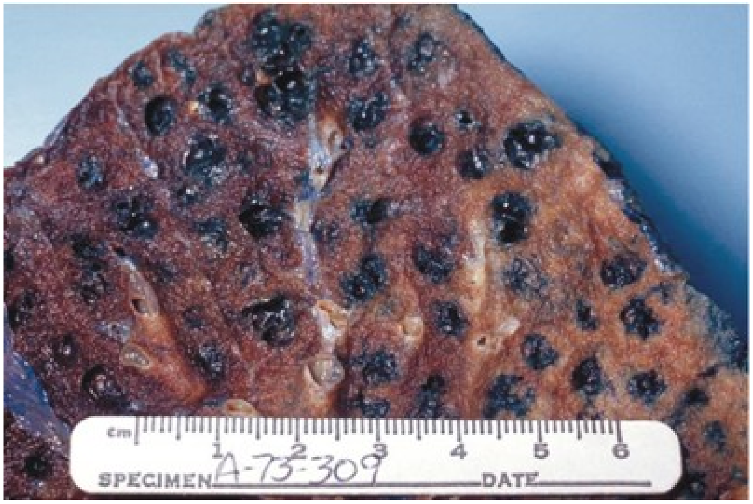

Figure 3.36: The inside of a lung showing the characteristics of emphysema due to smoking. Instead of alveoli, the cut surface shows multiple cavities lined by heavy black carbon deposits.

Bronchitis is an inflammation of the bronchi. Acute bronchitis is usually caused by viruses or bacteria and may last several days or weeks. Acute bronchitis is characterized by cough and phlegm (mucus) production. Symptoms are related to the inflammation of the airways and phlegm production, and include shortness of breath and wheezing. Chronic bronchitis is not necessarily caused by infection and is generally part of a syndrome called chronic obstructive pulmonary disease (COPD). Chronic bronchitis is defined clinically as a persistent cough that produces phlegm and mucus, for at least three months in two consecutive years.

Asthma is a chronic illness in which the airways narrow and becomes inflamed, as shown in **Figure** 3.37. Excessive amounts of mucus are also made by the lungs. Asthma often happens in response to one or more triggers. It may be triggered by exposure to an allergen such as mold, dust, or pet hair. It can also be caused by cold air, warm air, moist air, exercise, or emotional stress. In children, the most common triggers are viral illnesses such as those that cause the common cold. This airway narrowing causes symptoms such as wheezing, shortness of breath, chest tightness, and coughing. Some people with asthma, especially children, can become very frightened by the symptoms, which may cause even more breathing distress. Between asthma attacks, most patients feel well but can have mild symptoms and may remain short of

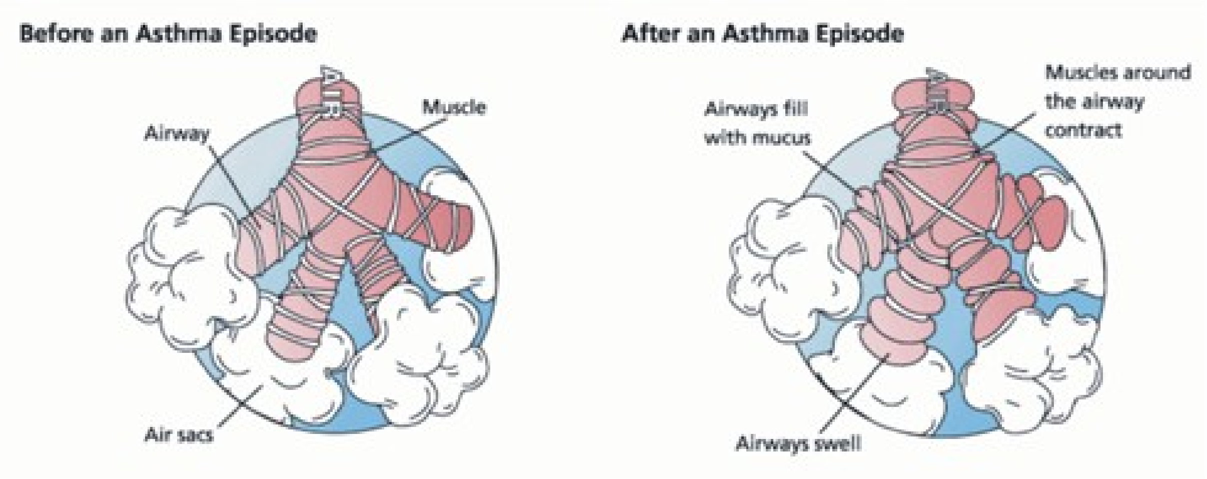

Figure 3.37: Asthma narrows the airways by causing allergy-induced spasms of surrounding muscles, narrowing of the airway, and excessive production of phlegm (mucus), which clogs the airways. The airway constriction responds to medicines called bronchodilators which relax the muscles. The feeling of breathlessness is somewhat like being able to breath only through a straw while walking.

breath after exercise for longer periods of time than a person who does not have asthma. The symptoms of asthma, which can range from mild to life threatening, can usually be controlled with a combination of medicines and environmental changes.

Public attention in the developed world has recently focused on asthma because of the increasing numbers of cases, affecting up to one in four children who live in cities.

Pneumonia is an illness in which the alveoli become inflamed and flooded with fluid. Effective gas exchange cannot happen across the alveoli membranes. Pneumonia can result from a variety of causes, including infection with bacteria, viruses, fungi, or parasites, and chemical or physical injury to the lungs. Symptoms of pneumonia include cough, chest pain, fever, and difficulty in breathing. Treatment depends on the cause of pneumonia; bacterial pneumonia is treated with antibiotics.

Pneumonia is a common illness which occurs in all age groups, and is a leading cause of death among the elderly and people who are chronically and terminally ill. Vaccines to prevent certain types of pneumonia are available.

Tuberculosis (TB) is a common and deadly infectious disease caused by a type of bacteria called *Mycobacterium tuberculosis.* TB most commonly attacks the lungs (as pulmonary TB) but can also affect the central nervous system, the lymphatic system, the circulatory system, the genitourinary system, bones, joints and even the skin.

Over one-third of the world's population has been exposed to the TB bacterium. Not everyone infected develops the disease, so TB infection without symptoms (called a latent infection) is most common. However, one in ten latent infections will progress to active TB disease, which, if left untreated, kills more than half of its victims.

The rise in HIV infections and the neglect of TB control programs have led to an increase in cases of tuberculosis. The development of drug-resistant strains has also contributed to this new epidemic. For example, between 2000 and 2004, about 20 percent of TB cases were resistant to standard antibiotic treatments. TB incidence varies widely, even in neighboring countries, apparently because of differences in health care system standards. A TB vaccine, called Bacille Calmette-Guérin (BCG), is available to people in some countries. The BCG is prepared from a strain of weakened live mycobacterium, which has lost its virulence in humans. The effectiveness of the BCG is a matter of debate among researchers, and the governments in some countries, including the United States, do not require people to get the BCG vaccination.

Lung cancer is a disease where epithelial (internal lining) tissue in the lung grows out of control. This leads to invasion of nearby tissue and growth of the tumor beyond the lungs. Lung cancer, which is the most common cause of cancer-related death in men and the second most common in women, is responsible for 1.3 million deaths worldwide every year The most common symptoms are shortness of breath, coughing (including coughing up blood), and weight loss.

The most common cause of lung cancer is exposure to tobacco smoke. The occurrence of lung cancer in non-smokers, who account for less than 10 percent of cases, appears to be due to a combination of genetic factors. Radon gas, asbestos, and air pollution may also contribute to lung cancer.

Asbestos is a mineral that was once used as a fire retardant in buildings and electrical wiring. The inhalation of asbestos fibers can cause a variety of lung diseases, including lung cancer. Tobacco smoking and exposure to asbestos greatly increase a person's chance of developing lung cancer.

Lesson Summary

- The main functions of lungs are to obtain oxygen, and to release carbon dioxide. Oxygen is drawn in through the respiratory tract and is then delivered to the blood in a process called external respiration. The exchange of gases between the blood and the cells of the body is celled internal respiration.
- The structures of the respiratory systems include the nose and nasal cavity, the pharynx, the larynx, (also called the voicebox), the trachea (also called the wind pipe), the right and left bronchi in the lungs, and the bronchioles that end in the alveoli.
- During inhalation, the diaphragm contracts, causing the volume of the chest cavity to increase. As a result, the air pressure within the lungs decreases. The pressure difference causes air to rush into the lungs. Relaxation of the diaphragm causes the lungs to recoil and air is pushed out of the lungs, which causes exhalation.
- Most of the carbon dioxide (about 70 percent) in the blood is in the form of bicarbonate (HCO_3^-). A small amount of carbon dioxide dissolves in the water in the plasma to form carbonic acid (H_2CO_3). When CO_2 enters the blood from body cells, it combines with water in the plasma to produce carbonic acid (H_2CO_3), which is then turned into bicarbonate (HCO_3^-). The bicarbonate is then picked up by a red blood cell and turned back in to carbonic acid. A water molecule (H_2O) is then taken away from the carbonic acid, and the remaining CO_2 molecule is expelled from the red blood cells and into the lungs.
- Emphysema is a chronic lung disease caused by loss of elasticity of the lung tissue. The destruction of elastic structures that support the alveoli and the capillaries that feed the alveoli cause them to become hard and stiff. It is often caused by smoking. Asthma is also a chronic condition, which is often triggered by such things as exposure to an allergen, cold air, warm air, moist air, exercise, or emotional stress. The airways can constrict and become inflamed, and an excessive amount of mucus is produced. Airway narrowing causes symptoms such as wheezing, shortness of breath, chest tightness, and coughing.

Review Questions

1. Identify the respiratory structures through which air flows.
2. How is the diaphragm involved in breathing?
3. Compare respiration and cellular respiration.
4. Outline how most carbon dioxide is carried in the blood.

5. Why is it important for a pregnant woman to know her Rhesus blood type, and the Rh blood type of the father of her baby?
6. What is the difference between internal and external respiration?
7. What happens during an asthma attack?
8. Outline how emphysema affects the absorption of oxygen.
9. Where does the exchange of oxygen occur in the lungs?
10. What factors regulate breathing rate?

Further Reading / Supplemental Links

- http://www.estrellamountain.edu/faculty/farabee/biobk/BioBookRESPSYS.html
- http://en.wikipedia.org

Vocabulary

alveoli Multi-lobed sacs in which most of the gas exchange occurs.

asthma A chronic illness in which the airways narrow and becomes inflamed.

bronchitis An inflammation of the bronchi.

diaphragm A muscle that is found below the lungs; contraction of the diaphragm causes the volume of the chest cavity to increase, and the air pressure within the lungs to decrease.

emphysema A chronic lung disease caused by loss of elasticity of the lung tissue.

external respiration Process in which oxygen is drawn in through the respiratory tract and is then delivered to the blood.

gas exchange The diffusion of gases between the alveoli and the blood passing in the lung capillaries; also the diffusion of gases from capillaries into cells, and from cells into capillaries throughout the body (peripheral gas exchange).

internal respiration The exchange of gases between the blood and the cells of the body.

larynx Found just below the point at which the pharynx splits into the trachea and the esophagus; also called the voice box.

lung cancer A disease where epithelial (internal lining) tissue in the lung grows out of control; leads to invasion of nearby tissue and growth of the tumor beyond the lungs.

lung volume (tidal volume) The average breath capacity of a person.

obstructive Conditions which lower the rate of the airflow into and out of the lungs, such as in asthma.

pharynx A long tube that is shared with the digestive system; both food and air pass through the pharynx.

pneumonia An illness in which the alveoli become inflamed and flooded with fluid.

respiration The transport of oxygen from the outside air to the cells of the body, and the transport of carbon dioxide in the opposite direction.

respiratory acidosis Condition in which arterial blood contains too much carbon dioxide, causing a drop in blood pH.

respiratory alkalosis Condition which results from increased respiration (or hyperventilation) which causes a drop in the amount of carbon dioxide in the blood plasma; the drop in carbon dioxide concentration causes the blood pH to rise.

respiratory disease The term for diseases of the lung, bronchial tubes, trachea and throat.

restrictive Conditions that cause a reduction in the functional volume of the lungs, such as emphysema.

trachea A long tube that leads down to the chest where it divides into the right and left bronchi in the lungs; also called the windpipe.

tuberculosis (TB) A common and deadly infectious disease caused by a type of bacteria called *Mycobacterium tuberculosis*; most commonly attacks the lungs, but can also affect the central nervous system, the lymphatic system, the circulatory system, the genitourinary system, bones, joints and even the skin.

Points to Consider

- How might the amount of oxygen in the air affect your respiratory and circulatory systems?
- Can you identify any structures that are part of both the respiratory and digestive systems?

Chapter 4

Excretory and Digestive Systems

4.1 Excretory System

Lesson Objectives

- Define homeostasis and excretion, and explain why they are necessary for life.
- Describe the urinary system, kidneys, and nephrons; summarize the processes involved in excretion.
- Identify roles of the kidneys in homeostasis.
- Name diseases of the urinary system, and explain how dialysis helps treat kidney failure.

Introduction

If you exercise on a hot day, you are likely to lose a lot of water in sweat. Then, for the next several hours, you may notice that you do not pass urine as often as normal and that your urine is darker than usual. Do you know why this happens? Your body is low on water and trying to reduce the amount of water lost in urine. How does the body know when it is low on water? How does it control the amount of water lost in urine? The answers to both questions are the kidneys and the glands that control them.

Homeostasis and Excretion

The kidneys are the body's main organs of homeostasis and excretion. Homeostasis is the body's attempt to maintain a constant internal environment. One of the major ways the body achieves homeostasis is through excretion. Excretion is the process of removing wastes and excess water from the body.

Homeostasis

Homeostasis is a fundamental characteristic of all living things. Internal body conditions must be kept within certain limits for the normal functioning of cells. Homeostasis involves keeping many internal factors at more or less constant levels. The factors include body temperature and properties of the blood. For example, the blood must have certain levels of acidity, salts, and nutrients in order for cells to function normally.

A variety of homeostatic mechanisms help maintain stability of the internal environment. Each mechanism involves the interaction of at last three components: a receptor, a control center, and an effector.

- The receptor senses changes in the internal environment and sends the information to the control center.
- The control center processes the information, determines the appropriate action, and sends a command to the effector.
- The effector responds to the command and changes conditions in the internal environment.

An example of a homeostatic mechanism in humans is the regulation of body temperature. This is represented by the diagram in **Figure** 4.1. Temperature receptors in the skin send information about skin temperature to the brain. The brain is the control center. It determines whether the temperature is too high or too low and sends appropriate commands to effectors that control body temperature. Effectors include blood vessels near the surface of the body. If the temperature is too high, the brain commands the blood vessels to dilate, which helps the body lose heat. If the temperature is too low, the brain commands the blood vessels to constrict, which helps the body retain heat. These actions help return body temperature to normal.

Negative Feedback and Body Temperature

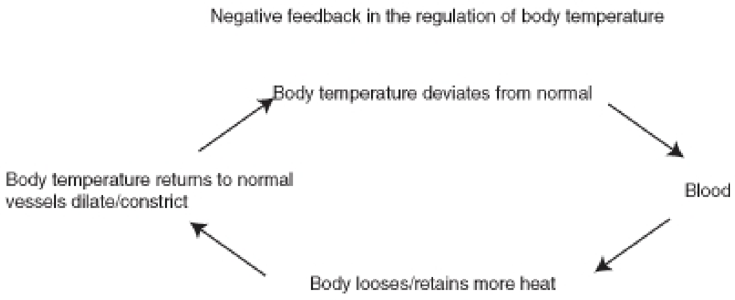
Negative feedback in the regulation of body temperature
Body temperature deviates from normal
Blood
Body looses/retains more heat
Body temperature returns to normal
vessels dilate/constrict

Figure 4.1: Regulation of body temperature is an example of negative feedback. When body temperature deviates from normal, this information feeds back to the brain and sets in motion changes that return body temperature to normal.

The regulation of body temperature is an example of negative feedback. Negative feedback is a type of homeostatic mechanism in which change in one direction results in a counteractive change in the opposite direction. Negative feedback reverses the direction of change to bring conditions back to normal. Most of the mechanisms that control homeostasis in the human body involve negative feedback.

Positive feedback mechanisms also exist, but they are not common in the human body. Positive feedback accelerates or amplifies a change and pushes levels farther away from normal. One example of a positive feedback mechanism in the body is blood clotting, which is described in the chapter titled *Circulatory and Respiratory Systems*.

If homeostasis is disturbed, a homeostatic imbalance results. This may result in cells getting too much or not enough of certain substances. Many diseases are caused by homeostatic imbalances. For example, diabetes mellitus is a disease in which the blood contains too much glucose. This can have serious consequences for cells throughout the body. It may lead to damaged blood vessels, heart disease, blindness, and kidney failure.

Excretion

Excretion is an essential process in all forms of life. When cells metabolize—or break down—nutrients, waste products are produced. For example, when cells metabolize proteins and nucleic acids, nitrogen wastes such as ammonia, urea and uric acid are produced. Ammonia is a toxic substance and must be removed from the blood and excreted from the body. Urea is removed through urine, which is produced in the kidney. Excretion is also necessary to remove excess water, salts, and many other substances from the body.

Although the kidneys are the main organs of excretion of wastes from the blood, several other organs are also involved in excretion, including the large intestine, liver, skin, and lungs.

- The large intestine eliminates solid wastes that remain after the digestion of food in the gastrointestinal tract (as discussed in Lesson 23.2: Digestive System).
- The liver breaks down excess amino acids in the blood to form ammonia, and then converts the ammonia to urea, a less toxic substance. The liver also breaks down other toxic substances in the blood, including alcohol and drugs.
- The skin eliminates water and salts in sweat.
- The lungs exhale water vapor and carbon dioxide.

Kidneys and Excretion

The kidneys are part of the urinary system. The kidneys work together with other urinary system organs in the function of excretion. The urinary system is shown in **Figure** 4.2.

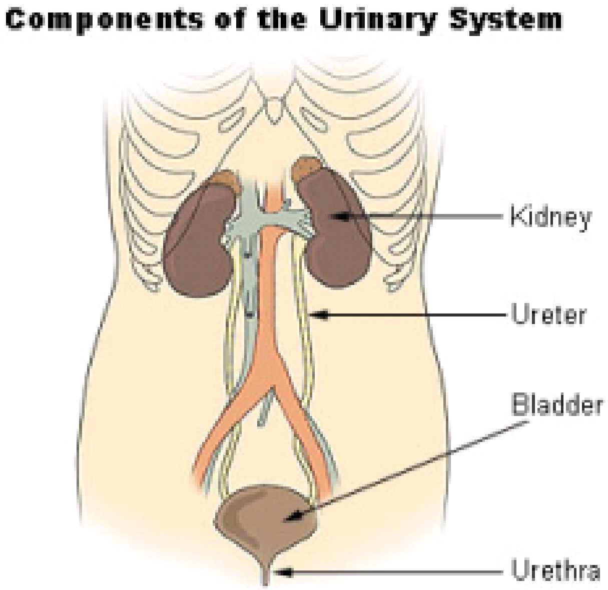

Figure 4.2: The urinary system.

Urinary System

In addition to the kidneys, the urinary system includes the ureters, bladder, and urethra. The main function of the urinary system is to filter waste products and excess water from the blood and remove them from the body. The two kidneys, which are described in detail below, filter the blood and form urine. Urine is the liquid waste product of the body that is excreted by the urinary system.

From the kidneys, urine enters the ureters, which carry it to the bladder. Each ureter is a muscular tube about 25 centimeters long. Peristaltic movements of the muscles of the ureter send urine to the bladder in small spurts.

The bladder is a hollow organ that stores urine. It can stretch to hold up to 500 milliliters. When the bladder is about half full, the stretching of the bladder sends a nerve impulse to the sphincter that controls the opening to the urethra. In response to the impulse, the sphincter relaxes and lets urine flow into the urethra.

The urethra is a muscular tube that carries urine out of the body. Urine leaves the body through another sphincter in the process of urination. This sphincter and the process of urination are normally under conscious control.

Kidneys (http://www.biologymad.com/resources/kidney.swf)

The kidneys participate in whole-body homeostasis. As mentioned above, one of the promary roles of the kidney is to remove nitrogenous wastes. The kidneys are a pair of bean-shaped, reddish brown organs about the size of a fist. They are located just above the waist at the back of the abdominal cavity, on either side of the spine. As shown in **Figure** 4.2, the kidneys are protected by the ribcage. They are also protected by a covering of tough connective tissues and two layers of fat, which help cushion them.

Located on top of each kidney is an adrenal gland, also shown in **Figure** 4.2. The two adrenal glands secrete several hormones. Hormones are chemical messengers in the body that regulate many body functions. The adrenal hormone aldosterone helps regulate kidney functions.

In **Figure** 4.3, you can see that the kidney has three layers. The outer layer is the renal cortex, and the middle layer is the renal medulla. The inner layer, the renal pelvis, is where the renal artery enters the kidney and the renal vein exits the kidney. The renal artery carries blood to the kidney to be filtered, and the renal vein carries the filtered blood away from the kidney. Structures in the kidney called nephrons are also seen in **Figure** 4.3. Each nephron extends from the cortex down into the medulla.

Nephrons (http://coe.fgcu.edu/faculty/greenep/kidney/index.html)

Nephrons are the structural and functional units of the kidneys. A single kidney may have more than a million nephrons. The diagram in **Figure** 4.4 represents an individual nephron and shows its main structures and functions. The structures include the glomerulus, Bowman's capsule, and renal tubule.

- The glomerulus is a cluster of arteries that filters substances out of the blood.
- Bowman's capsule is a cup-shaped structure around the glomerulus that collects the filtered substances.
- The renal tubule is a long, narrow tube surrounded by capillaries that reabsorbs many of the filtered substances and secretes other substances.

Filtration, Reabsorption, and Secretion

The renal arteries, which carry blood into the kidneys, branch into the capillaries of the glomerulus of each nephron. The pressure of blood moving through these capillaries forces some of the water and dissolved substances in the blood through the capillary walls and into Bowman's capsule. Bowman's capsule is composed of layers. The space between the layers, called Bowman's space, fills with the filtered substances.

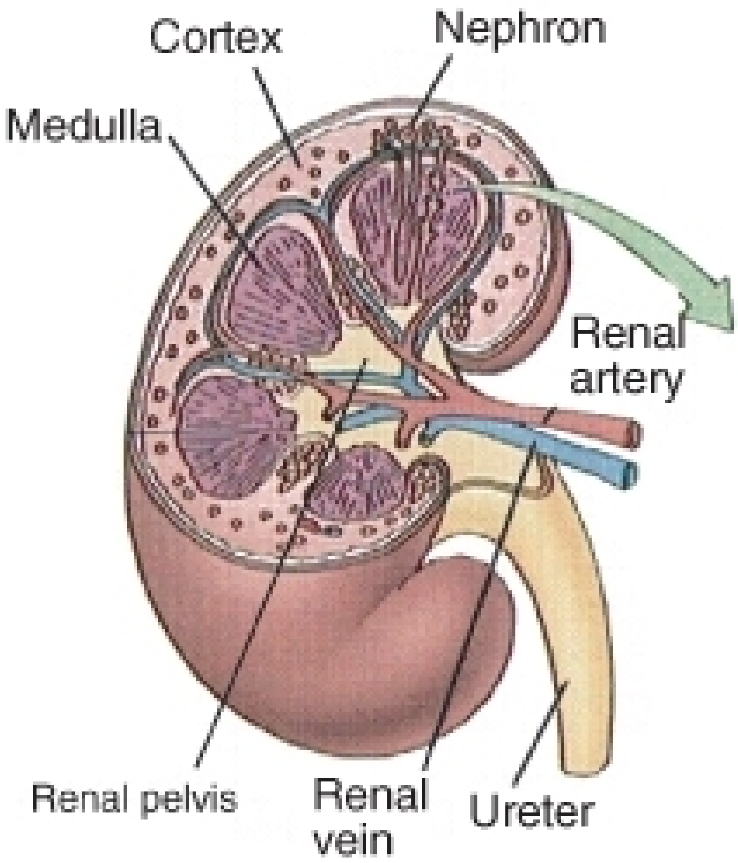

Figure 4.3: The human kidney.

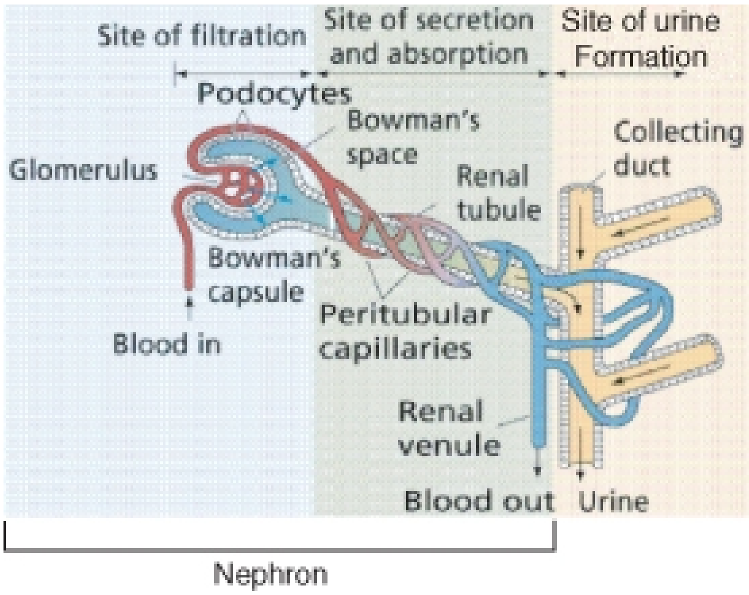

Figure 4.4: Nephron structures and functions.

The process of filtering substances from blood in the glomerulus is called filtration. The fluid that collects in Bowman's space is called filtrate. It is composed of water, salts, glucose, amino acids, and urea. Larger structures in the blood—including protein molecules, blood cells, and platelets—do not pass into Bowman's space. Instead, they return to the main circulation.

From Bowman's space, the filtrate passes into the renal tubule. The main function of the renal tubule is reabsorption. Reabsorption is the return of needed substances in the filtrate back to the bloodstream. It is necessary because some of the substances removed from the blood by filtration—including water, salts, glucose, and amino acids—are needed by the body. About 75 percent of these substances are reabsorbed in the renal tubule.

As shown in **Figure** 4.5, the renal tubule is divided into three parts: the proximal tubule, the Loop of Henle, and the distal tubule.

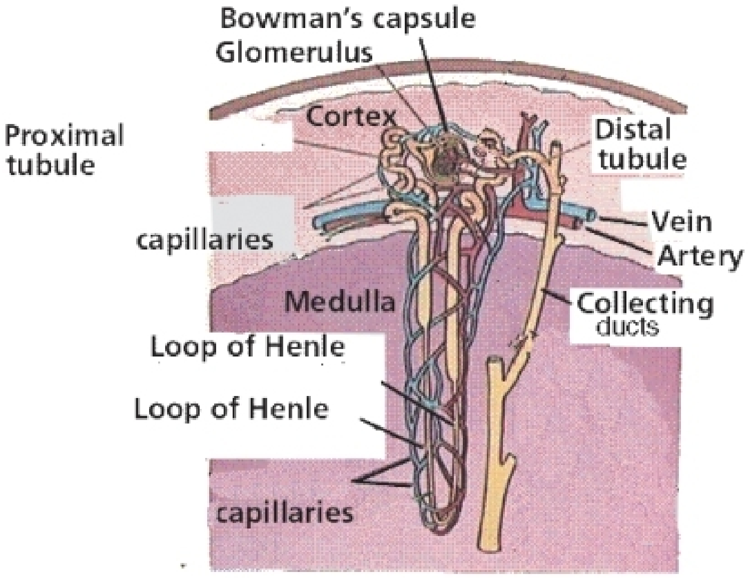

Figure 4.5: Parts of the renal tubule and other nephron structures.

- Filtrate first enters the proximal tubule. This is where that most reabsorption takes place. Tiny projections called microvilli line the proximal tubule and increase the surface area for reabsorption. From the proximal tubule, the filtrate passes through the loop of Henle.
- The loop of Henle carries the filtrate from the cortex down into the medulla and then back up to the cortex again. Its primary purpose is to reabsorb water and salt from the fluid. The remaining fluid enters the distal tubule.
- The distal tubule carries the fluid, now called tubular fluid, from the loop of Henle to a collecting duct. As it transports the fluid, the distal tubule also reabsorbs or secretes substances such as calcium and sodium. The process of secreting substances into the tubular fluid is called secretion.

Urine Formation

The collecting ducts are the site of urine formation. This process is crucial for water conservation in the body. The collecting ducts reabsorb water from tubular fluid and return it to the blood. The remaining fluid, called urine, has a smaller volume and a greater concentration than tubular fluid. From the collecting ducts, urine enters a ureter and is eventually excreted from the body.

The reabsorption of water by the collecting ducts is controlled by a negative feedback mechanism. The mechanism involves a hormone secreted by the pituitary gland, called antidiuretic hormone (ADH). ADH makes the collecting ducts more permeable to water, allowing more water to be reabsorbed from tubular fluid. When there is not enough water in the blood, more ADH is secreted, more water is reabsorbed from tubular fluid, and less water is excreted in urine. The opposite happens when there is too much water in the blood.

Kidneys and Homeostasis

The kidneys play many vital roles in homeostasis. As you have already read, the kidneys filter blood and excrete liquid waste. In fact, the kidneys filter all the blood in the body about 16 times a day, producing approximately 180 liters of filtrate and about 1.5 liters of urine. The kidneys also control the amount of water in the blood by excreting more or less water in urine.

Balancing the Blood

The kidneys are responsible for maintaining balance in the blood in other ways, as well. For example, they control the acid-base balance in the blood, mainly by secreting hydrogen ions into tubular fluid and reabsorbing bicarbonate ions from tubular fluid as needed. The kidneys also regulate blood concentrations of many other ions—including sodium, potassium, calcium, and magnesium—by the controlling the amounts that are excreted in urine.

Secreting Hormones

The kidneys also secrete various hormones to help maintain homeostasis. Hormones secreted by the kidneys include erythropoietin and rennin.

- Erythropoietin is secreted when the blood does not have enough red blood cells to carry adequate oxygen. The hormone stimulates the production of red blood cells by the bone marrow.
- Rennin is secreted when blood pressure falls. The hormone stimulates the secretion of aldosterone by the adrenal gland. Aldosterone, in turn, stimulates the kidneys to reabsorb more sodium ions and water. This increases the volume of the blood, which causes an increase in blood pressure.

Good Review Animations and Self Quiz: http://www.sumanasinc.com/webcontent/animations/content/kidney.html

Kidney Disease and Dialysis

A person can live a normal, healthy life with just one kidney. However, at least one kidney must function properly to maintain life. Diseases that threaten the health and functioning of the kidneys include kidney stones, infections, and diabetes.

Kidney Stones

Kidney stones are crystals of dissolved minerals that form in urine inside the kidneys. They may start out as small as a grain of salt and grow to be as large as a grapefruit. There may be one large stone or many small ones. Small kidney stones often pass undetected through the urinary tract and out of the body in urine. However, kidney stones may grow large enough before passing to block a ureter. This can cause a buildup of urine above the blockage and severe pain. Large kidney stones can sometimes be broken into smaller pieces that wash out of the urinary tract in urine. The stones are shattered by high-intensity sound waves focused on them from outside the body. Another alternative is to remove kidney stones surgically.

Infections

Bacterial infections of the urinary tract are very common. In fact, urinary tract infections (UTI) are the second most common type of bacterial infections seen by health care providers. Typical organisms that cause UTIs include *Escherichia coli* and *Staphylococcus saprophyticus*. The organisms may infect any part of the urinary tract.

The most common type of UTIs are bladder infections. They can be treated with antibiotics prescribed by a doctor. However, if a bladder infection is not treated, it may spread to the kidney and cause a kidney infection, or pyelonephritis. This is the most serious type of UTI. It can damage the kidney and interfere with normal kidney function. Kidney infections can also be treated with antibiotics but may require other treatments as well.

Diabetes

Two different types of diabetes can involve the kidneys: diabetes insipidus and diabetes mellitus. Diabetes insipidus is a disease characterized by the inability to concentrate urine. A person with this disease typically produces many liters of very dilute urine each day. Diabetes insipidus can be caused by a deficiency of ADH (antidiuretic hormone) or by the kidneys failing to respond to ADH. If the cause of diabetes insipidus can be treated, it may cure the disease.

In diabetes mellitus, the kidneys try to reduce the high glucose level in the blood by excreting more glucose in urine. This causes frequent urination and increased thirst. If blood glucose levels are not controlled by medication or diet, they may damage capillaries of the glomerulus and interfere with the kidney's ability to filter blood. Eventually, high glucose levels may lead to kidney failure, in which kidney function is greatly reduced. Kidney failure leads to high levels of urea and other wastes in the blood and may require treatment with dialysis.

Dialysis and Transplantation

Dialysis is a medical procedure in which blood is filtered with the help of a machine. One type of dialysis treatment is shown in **Figure** 4.6. Blood from the patient's vein enters the dialysis machine through a tube. Inside the machine, excess water, wastes, and other unneeded substances are filtered from the blood. The filtered blood is then returned to the patient's vein through another tube. A dialysis treatment usually lasts three to four hours and must be repeated three times a week. Dialysis is generally performed on patients who have kidney failure. Dialysis helps them stay alive, but does not cure their failing kidneys.

The only cure for most people with kidney failure is a kidney transplant. To be suitable for transplantation, the donated kidney must come from a donor who has the same blood and tissue types as the recipient. Even then, the recipient must take medication to suppress the immune system so it does not reject the new kidney.

Lesson Summary

- Homeostasis is the body's attempt to maintain a constant internal environment. Excretion helps achieve homeostasis by removing wastes, excess water, and other unneeded substances from the

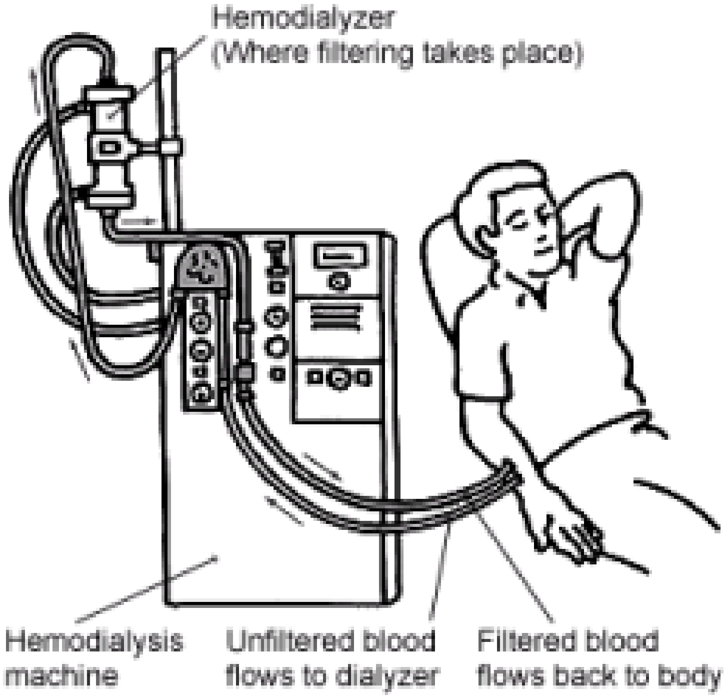
Hemodialyzer
(Where filtering takes place)
Hemodialysis machine
Unfiltered blood flows to dialyzer
Filtered blood flows back to body

Figure 4.6: Patient receiving dialysis treatment.

body. Both processes are essential for life.

- The urinary system includes the kidneys and other structures that excrete liquid waste. The kidneys are the main organs of excretion of wastes in the blood, and nephrons are structural and functional units of the kidneys. The kidneys filter blood, reabsorb and secrete substances, and form urine.
- The kidneys are the main organs of homeostasis. In addition to excretion, they regulate acid-base balance and ion concentrations in the blood. They also secrete hormones that control other body processes.
- Diseases of the urinary system include kidney stones, infections, and diabetes, which may lead to kidney failure. Kidney failure can be treated with dialysis, in which a machine filters the blood.

Review Questions

1. What are homeostasis and excretion?
2. Identify three organs of excretion and one substance that each organ excretes.
3. Why do the kidneys reabsorb some of the substances they filter from the blood?
4. Describe how urine forms in the collecting ducts of the kidneys.
5. How does ADH control the amount of water in urine? How is this an example of negative feedback?
6. Does an otherwise healthy person with just one kidney need dialysis? Why or why not?
7. Summarize the processes and structures involved in excretion by the kidneys.
8. Contrast the effects on the kidneys of diabetes insipidus and diabetes mellitus.

Further Reading / Supplemental Links

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- http://en.wikipedia.org

Vocabulary

bladder A hollow organ that stores urine.

Bowman's capsule A cup-shaped structure around the glomerulus that collects the filtered substances; part of the nephron.

control center Involved in maintaining homeostasis; processes the information, determines the appropriate action, and sends a command to the effector.

dialysis A medical procedure in which blood is filtered with the help of a machine.

effector Involved in maintaining homeostasis; responds to the command and changes conditions in the internal environment.

erythropoietin Hormone secreted by the kidney when the blood does not have enough red blood cells to carry adequate oxygen; stimulates the production of red blood cells by the bone marrow.

excretion The process of removing wastes and excess water from the body.

filtration The process of filtering substances from blood in the glomerulus.

glomerulus Part of the nephron; a cluster of arteries that filters substances out of the blood.

homeostasis The body's attempt to maintain a constant internal environment.

kidney Organ that filters the blood and forms urine.

kidney stones Crystals of dissolved minerals that form in urine inside the kidneys.

loop of Henle Carries the filtrate from the cortex down into the medulla and then back up to the cortex again; primary purpose is to reabsorb water and salt from the fluid.

negative feedback A type of homeostatic mechanism in which change in one direction results in a counteractive change in the opposite direction; reverses the direction of change to bring conditions back to normal.

nephrons The structural and functional units of the kidneys; includes the glomerulus, Bowman's capsule, and renal tubule.

positive feedback Accelerates or amplifies a change and pushes levels farther away from normal; not common in the human body.

reabsorption The return of needed substances in the filtrate back to the bloodstream.

receptor Involved in maintaining homeostasis; senses changes in the internal environment and sends the information to the control center.

renal tubule A long, narrow tube surrounded by capillaries that reabsorbs many of the filtered substances and secretes other substances; part of the nephron.

rennin Hormone secreted by kidney when blood pressure falls; stimulates the secretion of aldosterone by the adrenal gland. Aldosterone, in turn, stimulates the kidneys to reabsorb more sodium ions and water.

urethra A muscular tube that carries urine out of the body.

urinary system System in which the main function is to filter waste products and excess water from the blood and remove them from the body.

urine The liquid waste product of the body that is excreted by the urinary system.

Points to Consider

- A transplanted kidney may be rejected unless medication is taken to suppress the immune system. Why does the immune system reject transplanted organs?
- How does the immune system recognize transplanted organs as foreign to the body?
- What happens when the immune system ‘‘attacks'' a transplanted organ?

4.2 Digestive System

Lesson Objectives

- Describe the organs and major functions of the digestive system.
- Explain how the mouth, esophagus, and stomach start the digestion of food.
- Explain how the small intestine completes digestion and absorbs nutrients.
- State the functions of the large intestine and the roles of intestinal bacteria.
- Identify and describe diseases of the digestive system.

Introduction

Suppose you are studying and having trouble concentrating. You decide to eat an apple for energy. How does energy stored in the apple get into your cells? What organs and processes break down the apple into nutrients that the body can use for fuel? What organs and processes let the nutrients enter your bloodstream so they can travel to the cells where they are needed? The basic processes involved are digestion and absorption. The organs involved are the organs of the digestive system.

Organs and Functions of the Digestive System

Organs that make up the digestive system are shown in **Figure** 4.7. Most of the organs form the gastrointestinal tract. Other digestive organs are called accessory organs. As you read about the organs below, refer to **Figure** 4.7 for reference.

Gastrointestinal Tract

The gastrointestinal (GI) tract is a long tube that connects the mouth with the anus. It is more than 9 meters long in adults. The GI tract can be divided into an upper and lower part. The upper GI tract includes the mouth, esophagus, and stomach. The lower GI tract includes the small and large intestines. Food enters the mouth, passes through the upper and lower GI tracts, and then exits the body as feces through the anus.

The organs of the GI tract are covered by two layers of muscles that enable peristalsis. Peristalsis is a rapid, involuntary, wave-like contraction of muscles. It pushes food through the GI tract. The inside of GI tract is lined with mucous membranes. Mucous membranes are moist tissues that can secrete and absorb substances. The ability to secrete and absorb substances is necessary for the functions of the digestive system. See http://en.wikipedia.org/wiki/File:Peristalsis.gif for an animation of peristalsis.

Accessory Organs of the Digestive System

In the lower GI tract, additional organs play important roles in digestion. They are called accessory organs. Food does not pass through them, but they make or store substances needed for digestion. The accessory organs are the liver, gall bladder, and pancreas.

- The liver is a large organ next to the stomach. It produces digestive substances that are carried by ducts, or tubes, to the small intestine and gall bladder.
- The gall bladder is a small, pear-shaped structure below the liver. It stores substances from the liver until they are needed by the small intestine.

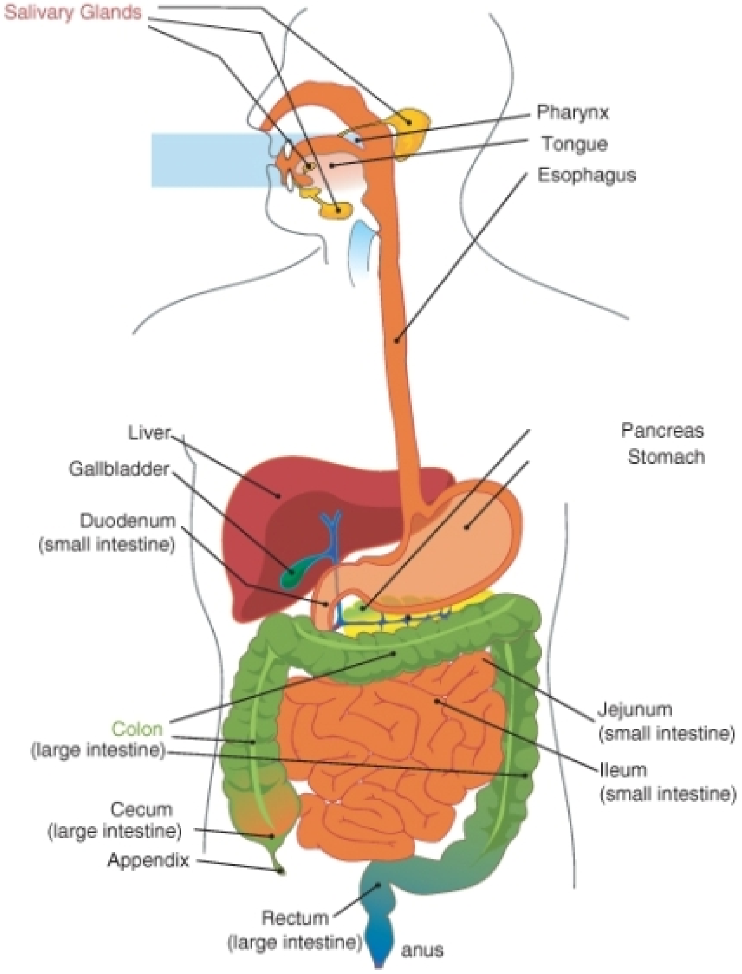

Figure 4.7: Organs of the digestive system.

- The pancreas is a gland below the stomach. It produces digestive substances that are carried by a duct to the small intestine.

The Liver

The liver is a vital organ that has many functions, including detoxification of blood, protein synthesis, and production of biochemicals necessary for digestion. The liver is also involved in glucose balance. The liver produces bile which breaks down lipids.

The liver performs several roles in carbohydrate metabolism, which help in the balance of blood glucose levels:

- Gluconeogenesis: the synthesis of glucose from certain amino acids, lactate or glycerol
- Glycogenolysis: the breakdown of glycogen into glucose
- Glycogenesis: the formation of glycogen from glucose.

The liver is one of the most important organs in the body when it comes to blood filtering and detoxification. The liver is involved in getting rid of foreign substances and toxins, especially from the gut. The toxins are usually excreted in bile or urine. Breaking down toxins is referred to as drug metabolism, and is usually done using specialized enzymes produced in the liver. Most of the blood being filtered by the liver is from the portal vein, which carries blood from the intestines. The liver can remove a broad range of microorganisms such as bacteria, fungi, viruses and parasites from the blood. Infections and parasites can come from contaminated water and food, and then find their way into your gut and blood stream. Luckily the blood then goes to the liver for filtering.

The liver also performs several roles in lipid metabolism including cholesterol synthesis and the production of triglycerides (fats). The liver produces coagulation factors I (fibrinogen), II (prothrombin), V, VII, IX, X and XI, as well as protein C, protein S and antithrombin.

Functions of the Digestive System

The digestive system has three main functions: digestion of food, absorption of nutrients, and elimination of solid waste. Digestion is the process of breaking down food into components the body can absorb. There are two types of digestion: mechanical and chemical.

- Mechanical digestion is the physical breakdown of chunks of food into smaller pieces. It takes place mainly in the mouth and stomach.
- Chemical digestion is the chemical breakdown of large, complex food molecules into smaller, simpler nutrient molecules that can be absorbed by the blood. It takes place mainly in the small intestine.

Chemical digestion could not take place without the help of digestive enzymes. Enzymes are substances that speed up chemical reactions. Digestive enzymes speed up the reactions of chemical digestion. Digestive enzymes are secreted by glands in the mucous membranes of the mouth, stomach, small intestine, and pancreas. Different digestive enzymes help break down different types of food molecules, including carbohydrates, proteins, and lipids.

The name of a digestive enzyme typically ends with the suffix -*ase*, which means ‘‘enzyme”. The rest of the name refers to the type of food molecules the enzyme helps digest. For example, the enzyme lipase helps digest lipid molecules, and the enzyme lactase helps digest molecules of the sugar lactose.

After food is digested, the resulting nutrients are absorbed. Absorption is the process in which substances pass into the blood stream, where they can circulate throughout the body. Absorption occurs mainly in the small intestine. Any remaining indigestible matter that cannot be absorbed passes into the large intestine as waste. The waste later passes out of the body through the anus in the process of elimination.

The Start of Digestion: The Mouth to the Stomach

The upper GI tract is the primary site of mechanical digestion. The chemical digestion of carbohydrates and proteins also begins in the upper GI tract.

The Mouth

The mouth is the first organ in the digestive tract, but digestion may start even before you put the first bite of food in your mouth. Why? The sight or aroma of an appetizing dish can stimulate the release of digestive enzymes by salivary glands inside your mouth. The major salivary enzyme is amylase. Once you start eating, amylase begins the chemical digestion of carbohydrates in the food. It helps break down complex starch molecules into simpler sugar molecules.

The mouth also plays an important role in mechanical digestion. The teeth help to digest food mechanically by breaking it into smaller pieces. Human teeth have different shapes and functions. As you can see in **Figure** 4.8, the incisors and canines at the front of the mouth are relatively thin and sharp. They shear and tear food when you bite into it. The premolars and molars at the back of the mouth are larger and broader. They grind food into smaller pieces as you chew.

Saliva from the salivary glands moistens the food and makes it easier to chew. The muscular tongue helps mix the food with saliva and the enzymes it contains. When you swallow, the lump of chewed food, now called a bolus, passes into the pharynx.

The pharynx connects the mouth to the rest of the digestive tract. It also connects the mouth and nose to the rest of the respiratory system. As food is pushed to the back of the mouth by the tongue, it sets off an automatic response that closes the pharynx off from the respiratory system. This prevents you from accidentally inhaling food when you swallow.

Esophagus

From the pharynx, the bolus moves into the esophagus. The esophagus is a narrow tube about 20 centimeters long in adults. It begins at the pharynx, passes through the chest, and ends at the opening to the stomach. The function of the esophagus is to pass food from the mouth to the stomach. This takes only a few seconds. The esophagus does not produce digestive enzymes and does not have any other digestive functions.

Food moves through the esophagus due to peristalsis. At the end of the esophagus, a muscle called a sphincter controls the entrance to the stomach. The sphincter opens to let food into the stomach and then closes again to prevent the food from passing back into the esophagus.

Stomach

The stomach is a saclike organ located between the end of the esophagus and the beginning of the small intestine. In the stomach, food is further digested both mechanically and chemically. Churning movements

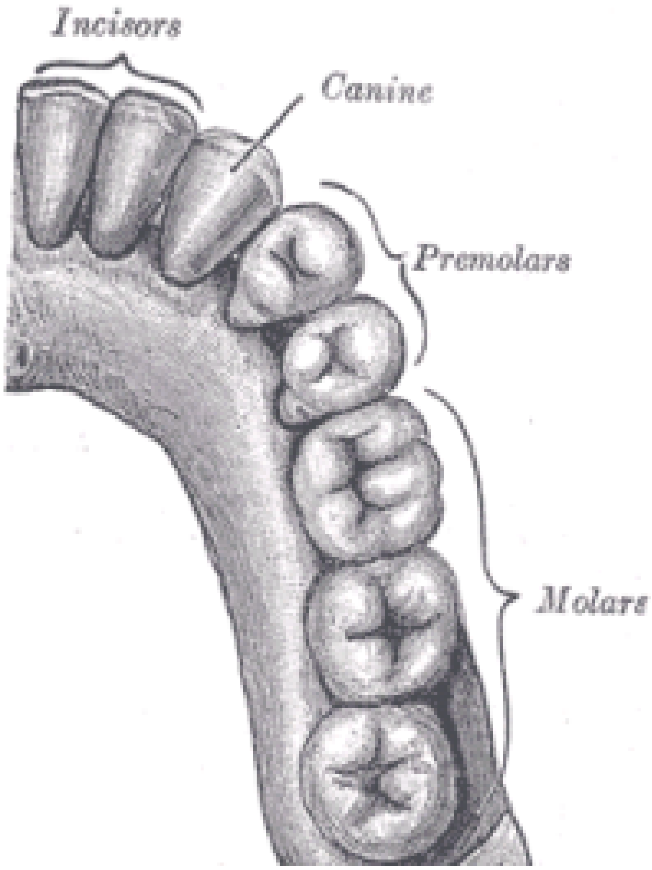

Figure 4.8: Types of human teeth.

of the stomach's thick muscular walls break down food mechanically. The churning movements also mix the food with fluids secreted by the stomach. These fluids include hydrochloric acid and digestive enzymes.

- Hydrochloric acid gives the stomach a very acidic environment. This helps destroy any bacteria that have entered the stomach in foods or beverages. An acidic environment is also needed for the stomach's digestive enzymes to work.
- Digestive enzymes secreted in the stomach help break down proteins into smaller molecules called peptides. The main digestive enzyme in the stomach is pepsin.

Water, alcohol, salt, and simple sugars can be absorbed through the lining of the stomach. Most other substances need further digestion in the small intestine before they can be absorbed. The stomach stores the food until the small intestine is ready to receive it. It may hold up to four liters of food when fully expanded. When the small intestine is empty, a sphincter opens between the stomach and small intestine. This allows the partially digested food, now called chyme, to enter the small intestine.

Digestion and Absorption: The Small Intestine

The small intestine is narrow tube about seven meters long in adults. It is the site of most chemical digestion and virtually all absorption. As you can see from Figure 1, the small intestine is much longer than the large intestine. It is called "small" because it is smaller in diameter than the large intestine. Like the rest of the GI tract, the small intestine pushes food along with peristalsis. The small intestine is made up of three parts: the duodenum, jejunum, and ileum. Each part has a different function.

Digestion in the Small Intestine

The **duodenum** is the first part of the small intestine. It is only about 25 cm long, but most chemical digestion occurs here. Many enzymes are active in the duodenum, and several are listed in **Table** 4.1. Some of the enzymes are produced by the duodenum. The rest are produced by the pancreas and secreted into the duodenum.

Table 4.1: **Digestive Enzymes Active in the Duodenum**

Name of Enzyme	Nutrient It Digests	Site of Production
Amylase	carbohydrates	pancreas
Trypsin	proteins	pancreas
Lipase	lipids	pancreas
Maltase	carbohydrates	small intestine
Peptidase	proteins	small intestine
Lipase	lipids	small intestine

How does the pancreas "know" when to secrete enzymes into the small intestine? The pancreas is controlled by compounds called hormones. Hormones are chemical messengers in the body. They regulate many body functions, including secretion of digestive enzymes. When food enters the stomach, a hormone called gastrin is secreted by the stomach. Gastrin, in turn, stimulates the pancreas to secrete its digestive enzymes.

The liver produces fluid called bile, which is secreted into the duodenum. Some bile goes to the gall bladder, where it is stored and becomes more concentrated. In the duodenum, bile breaks up large globules of lipids into smaller globules that are easier for lipase enzymes to break down chemically.

Bile also reduces the acidity of the chyme entering from the highly acidic stomach. This is important for digestion, because digestive enzymes in the duodenum require a neutral environment in order to work. The pancreas also contributes to the neutral environment of the duodenum by secreting bicarbonate, a basic substance that neutralizes acid.

Absorption in the Small Intestine

The **jejunum** is the second part of the small intestine. It is about 2.5 meters long. This is where most nutrients are absorbed into the blood.

As shown in **Figure** 4.9, the mucous membrane lining the jejunum is covered with microscopic, fingerlike projections called **villi** (singular: villus). Each villus, in turn, has thousands of even smaller projections called microvilli (singular: microvillus). The villi contain capillaries, which are tiny blood vessels. Nutrients are absorbed into these capillaries across the surface of the villi and microvilli. Because there are millions of these tiny projections, they greatly increase the surface area for absorption. In fact, villi and microvilli increase the absorptive surface of the small intestine to the size of a tennis court! This allows far greater absorption of nutrients.

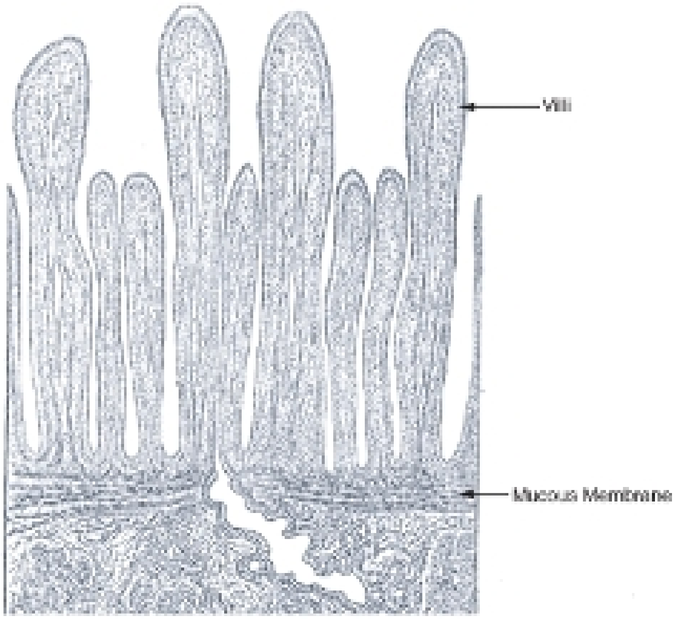

Figure 4.9: Magnified image of villi lining the jejunum (small intestine).

The **ileum** is the third part of the small intestine. It is about 3.5 meters long. A few remaining nutrients are absorbed in the ileum. Salts that form from liver bile are also absorbed there. Like the jejunum, the ileum is covered with villi and microvilli that increase the area for absorption.

The Large Intestine and Its Functions

From the small intestine, any remaining food waste passes into the large intestine. The large intestine is a relatively wide tube that connects the small intestine with the anus. It is about 1.5 meters long. The large intestine consists of three parts: the cecum, colon, and rectum.

Absorption of Water and Elimination of Wastes

The cecum is the first part of the large intestine, where waste enters from the small intestine. The waste is in a liquid state. As the waste passes through the colon, which is the second part of the large intestine, excess water is absorbed. After the excess water is absorbed, the remaining solid waste is called feces. Feces contain indigestible food substances such as fiber.

Feces accumulate in the rectum, which is the third part of the large intestine. As the rectum fills, the feces become compacted. The feces are stored in the rectum until they are eliminated from the body. A sphincter controls the anus and opens to let feces through to the outside. It normally takes from 12 to 24 hours for wastes to enter the cecum, move through colon, accumulate in the rectum, and pass from the body as feces.

Bacteria in the Large Intestine

Other functions of the large intestine are to provide a home for intestinal bacteria and to absorb the vitamins they produce. Trillions of bacteria normally live in the large intestine. Some of these bacteria are harmful to the body if they grow out of control. However, most of the bacteria are helpful. They produce several vitamins, including vitamins B_{12} and K. Intestinal bacteria play other helpful roles, as well. For example, they:

- control the growth of harmful bacteria.
- break down toxins before they can poison the body.
- break down indigestible food components.
- produce substances that help prevent colon cancer.

Diseases of the Digestive System

A number of diseases can affect the entire gastrointestinal tract. Other diseases affect particular organs of the GI tract. Still others affect accessory organs of the digestive system.

Diseases of the Gastrointestinal Tract

A group of diseases that affect the GI tract is called inflammatory bowel disease. Inflammatory bowel disease is inflammation of the large intestine and, in some cases, other parts of the GI tract. Inflammation is a normal reaction of the immune system to injury or infection that causes swelling, redness, and pain.

The two main forms of inflammatory bowel disease are Crohn’s disease and ulcerative colitis. Both have similar symptoms, including abdominal pain, diarrhea, and weight loss. Crohn’s disease is caused by the immune system reacting to the body’s own tissues, but the cause of ulcerative colitis is not known. A tendency to develop the diseases may be inherited. Ulcerative colitis is confined to the colon and sometimes can be cured with surgery. Crohn’s disease may occur anywhere in the GI tract and has no known cure, although treatment can control the symptoms.

Food allergies can also affect the entire GI tract. Food allergies are disorders that occur when the immune system reacts to substances in food as though they were harmful “foreign invaders.” Foods that are most likely to cause allergies are nuts, eggs, milk, fish, and shellfish. Symptoms of food allergies may include tingling in the mouth, vomiting, and diarrhea. Food allergies can also cause skin rashes and difficulty breathing. An estimated eight percent of children and two percent of adults have food allergies.

Diseases of the Stomach and Esophagus

A layer of mucus normally protects the lining of the stomach from damage by hydrochloric acid. An infection by bacteria of the species *Helicobacter pylori* can weaken this mucus layer, allowing acid to get through to the delicate mucous membranes underneath. The acid may cause gastritis or stomach ulcers, both of which can be treated with medication.

- Gastritis is inflammation of the lining of the stomach. It causes abdominal pain.
- A stomach ulcer is a sore in the lining of the stomach. It causes severe abdominal pain and bleeding.

Stomach acid may also damage the lining of the esophagus. This can occur when the sphincter between the stomach and esophagus does not close properly. This lets acid from the stomach enter the esophagus. The acid may cause esophagitis, or inflammation of the esophagus. A common symptom of esophagitis is heartburn, which is a painful, burning sensation in the throat or chest. Esophagitis can be treated with medication and changes in diet. It is important to treat the condition because it sometimes leads to cancer of the esophagus if not treated.

Diseases of the Small Intestine

Diseases that affect the small intestine include ulcers, infections, and celiac disease. Ulcers of the small intestine occur mainly in the duodenum, because stomach acid enters the duodenum during digestion. If an infection by *Helicobacter pylori* weakens the mucous layer in the duodenum, the stomach acid can damage the mucous membranes underneath. Symptoms and treatment of duodenal ulcers are similar to those of stomach ulcers.

Other bacteria may also cause infections in the small intestine, including Salmonella and *E. coli*. The bacteria can enter the body in contaminated foods or beverages. Symptoms of bacterial infections include abdominal pain, cramping, vomiting, and diarrhea. Such infections typically clear up on their own without medical treatment.

Celiac disease is an immune reaction to a food protein called gluten, which is found in grains. A tendency to have celiac disease can be inherited. Symptoms of the disease include abdominal pain, diarrhea, and bloating. The symptoms can be prevented by eating a gluten-free diet, but there is no cure for the disease.

Diseases of the Large Intestine

Diseases that affect the large intestine include irritable bowel syndrome, colitis, and appendicitis. Irritable bowel syndrome (IBS) is a disorder in which the large intestine is easily irritated. It is one of the most common gastrointestinal disorders. The cause of IBS is unknown, but may be due to excessive bacteria in the intestine. Symptoms of the disorder include abdominal pain, cramping, constipation, and diarrhea. Symptoms can often be controlled with medication, stress management, and changes in diet. However, there is no cure for IBS.

Colitis is inflammation of the colon. It has many possible causes, ranging from bacterial infections to immune reactions against the body's own tissues. Symptoms of colitis include pain and tenderness in the abdomen. Treatment of colitis may include medication, surgery, and changes in diet.

Appendicitis is inflammation of the appendix. It is most common in children and teens. The appendix is a small, fingerlike pouch that extends from the cecum (see **Figure** 4.7). Inflammation of the appendix is usually caused by a bacterial infection. Symptoms include abdominal pain, loss of appetite, fever, and vomiting. Appendicitis is most often treated with surgery to remove the infected appendix. Without treatment, an infected appendix can be fatal.

Diseases of the Accessory Organs

Accessory organs of digestion can also be affected by disease, and this may interfere with normal digestion. A disease that affects the pancreas is cystic fibrosis. Cystic fibrosis (CF) is an inherited disease in which the body produces abnormally thick and sticky mucous. In the pancreas, the mucus blocks the duct to the duodenum, preventing pancreatic enzymes from reaching it. As a result, proteins and lipids cannot be digested properly. People with CF may take digestive enzymes by mouth to improve their digestion. However, the disease has no known cure. (For more information on CF, see chapter titled *Human Genetics.*)

Hepatitis is inflammation of the liver. It is usually caused by a viral infection. Several different viruses can cause hepatitis. Some of the viruses spread through contaminated foods or beverages, others through sexual contact. Symptoms of hepatitis include fever, headache, vomiting, and abdominal pain. Another symptom is jaundice, which is yellowing of the skin and eyes. If the symptoms are mild, the disease may clear up without treatment. If the symptoms are more severe, the disease may damage the liver so it can no longer produce bile. This interferes with the digestion of lipids. Medications are available to treat hepatitis. Some types of hepatitis can also be prevented with vaccines.

Gall bladder problems occur mainly in adults. They are often caused by gall stones (**Figure** 4.10). Gall stones are crystals that form in the bile in the gall bladder. There are many possible reasons why gall stones form, including abnormal body chemistry and too much fat in the diet. Gall stones start out as small as a grain of sand but may grow to the size of a golf ball. There may be one large stone or many small ones. If gall stones block the duct that carries bile to the duodenum, they may cause inflammation of the gall bladder and severe abdominal pain. Generally, the only way to treat these problems is to surgically remove the gall stones or the entire gall bladder.

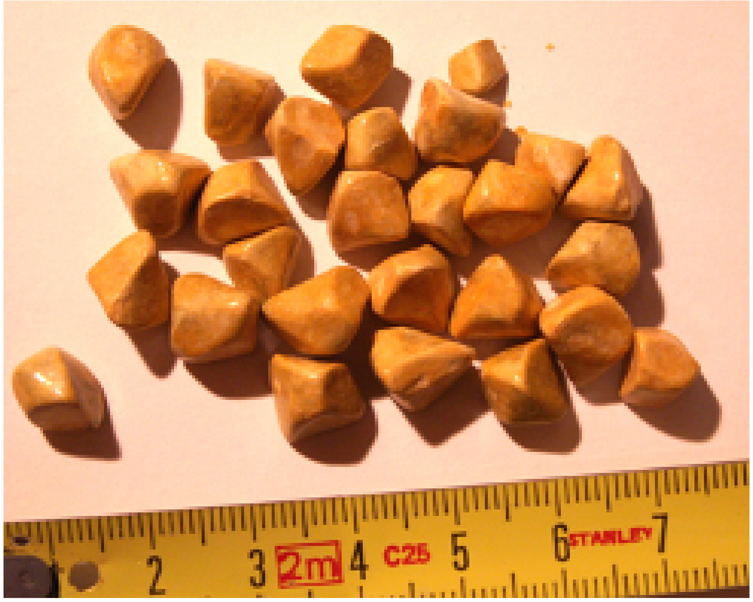

Figure 4.10: Gall stones.

Lesson Summary

- The digestive system includes the gastrointestinal tract and accessory organs such as the pancreas. The major functions of the digestive system are to digest food, absorb nutrients, and eliminate solid waste.

- Both mechanical and chemical digestion of food start in the mouth. The esophagus carries the food to the stomach, and the stomach continues mechanical and chemical digestion.
- Most chemical digestion takes place in the small intestine with the help of several digestive enzymes. Virtually all absorption of nutrients also takes place in the small intestine.
- The large intestine removes excess water from waste and eliminates waste from the body. It also provides a home for helpful intestinal bacteria.
- Many diseases affect the digestive system and may interfere with digestion. They include food allergies, infections, and inherited conditions.

Review Questions

1. Name, in sequence, the digestive organs that food passes through in the gastrointestinal tract, from the mouth to the anus.
2. Describe two ways that the mouth helps digest food.
3. How do villi and microvilli help the small intestine absorb nutrients?
4. What are two functions of helpful bacteria in the large intestine?
5. Describe what happens to carbohydrates as they pass through the organs of the GI tract.
6. Antibiotics are medications that destroy bacteria. Explain how antibiotics might help treat stomach ulcers.
7. Why is it important for digestive system functions that mucous membranes can secrete and absorb substances?
8. Compare and contrast two digestive enzymes that work in the duodenum.

Further Reading / Supplemental Links

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Vocabulary

absorption The process in which substances pass into the blood stream, where they can circulate throughout the body; occurs mainly in the small intestine.

amylase The major salivary enzyme is amylase; begins the chemical digestion of carbohydrates in the food; helps break down complex starch molecules into simpler sugar molecules.

cecum The first part of the large intestine, where waste enters from the small intestine.

celiac disease An immune reaction to a food protein called gluten, which is found in grains.

chemical digestion The chemical breakdown of large, complex food molecules into smaller, simpler nutrient molecules that can be absorbed by the blood; takes place mainly in the small intestine.

colon The second part of the large intestine, where excess water is absorbed. After the excess water is absorbed, the remaining solid waste is called feces.

duodenum The first part of the small intestine; site where most chemical digestion occurs.

esophagus A narrow tube - begins at the pharynx, passes through the chest, and ends at the opening to the stomach. The function of the esophagus is to pass food from the mouth to the stomach.

gall bladder A small, pear-shaped structure below the liver; stores substances from the liver until they are needed by the small intestine.

gastritis Inflammation of the lining of the stomach.

gastrointestinal (GI) tract Organ of the digestive system; a long tube that connects the mouth with the anus.

ileum The third part of the small intestine. A few remaining nutrients are absorbed in the ileum, as are salts that form from liver bile.

inflammatory bowel disease Inflammation of the large intestine and, in some cases, other parts of the GI tract; includes Crohn's disease and ulcerative colitis.

irritable bowel syndrome (IBS) A disorder in which the large intestine is easily irritated.

jejunum The second part of the small intestine; where most nutrients are absorbed into the blood.

large intestine A relatively wide tube that connects the small intestine with the anus; consists of three parts: the cecum, colon, and rectum.

liver A large organ next to the stomach; produces digestive substances that are carried by ducts, or tubes, to the small intestine and gall bladder.

lower GI tract Segment of the GI tract that includes the small and large intestines.

mechanical digestion The physical breakdown of chunks of food into smaller pieces; takes place mainly in the mouth and stomach.

mucous membranes Moist tissues that can secrete and absorb substances.

pancreas A gland below the stomach; produces digestive substances that are carried by a duct to the small intestine.

peristalsis A rapid, involuntary, wave-like contraction of muscles; pushes food through the GI tract.

pharynx Connects the mouth to the rest of the digestive tract; also connects the mouth and nose to the rest of the respiratory system.

rectum The third part of the large intestine; where feces accumulates. As the rectum fills, the feces become compacted. The feces are stored in the rectum until they are eliminated from the body.

small intestine A narrow tube leading away from the stomach; made up of three parts: the duodenum, jejunum, and ileum; the site of most chemical digestion and virtually all absorption.

stomach A saclike organ located between the end of the esophagus and the beginning of the small intestine. In the stomach, food is further digested both mechanically and chemically.

stomach ulcer A sore in the lining of the stomach.

upper GI tract Segment of the GI tract that includes the mouth, esophagus, and stomach.

Points to Consider

- The large intestine eliminates the waste that remains after food is digested. More waste is produced when cells break down nutrients for energy and building materials. How is this waste removed from the body? Is it eliminated by the large intestine? Is it removed in some other way?

4.3 Food and Nutrients

Lesson Objectives

- Identify classes of macronutrients and describe their roles in the body.
- Describe balanced eating and explain how it helps prevent obesity.
- State functions and food sources of vitamins and minerals.
- Describe eating disorders, their causes, and treatment.

Introduction

Did you ever hear the saying, "You are what you eat"? It's not just a saying. It's actually true. What you eat plays an important role in your health. Eating a variety of healthful foods promotes good physical health and provides energy for growth and activity. Many common diseases and their symptoms can be prevented or helped with healthful eating. Knowing what your body needs can help you choose foods to meet those needs.

Nutrients, Energy, and Building Materials

Nutrients are chemical elements or compounds that the body needs for normal functioning and good health. There are six main classes of nutrients: carbohydrates, proteins, lipids, water, vitamins, and minerals. The body needs these nutrients for three basic purposes: energy, building materials, and control of body processes.

A steady supply of energy is needed by cells for all body functions. Carbohydrates, proteins, and lipids provide this energy. Chemical bonds in molecules of these nutrients contain energy. When the bonds are broken during digestion to form simpler molecules, the energy is released. Energy is measured in units called kilocalories (kcal), commonly referred to as Calories.

Molecules that make up the body are continuously broken down or used up, so they must be replaced. Some nutrients, particularly proteins, provide the building materials for this purpose. Other nutrients—including proteins, vitamins, and minerals—are needed to regulate body processes. One way is by helping to form enzymes. Enzymes are compounds that control the rate of chemical reactions in the body.

Nutrients can be classified in two groups based on how much of them the body needs:

- **Macronutrients** are nutrients that the body needs in relatively large amounts. They include carbohydrates, proteins, lipids, and water.
- **Micronutrients** are nutrients the body needs in relatively small amounts. They include vitamins and minerals.

The exact amount of a macronutrient an individual needs depends on many factors, including gender and age. Recommended daily intakes of three macronutrients for young people of both genders are shown in **Table** 4.2.

Table 4.2: **Recommended Daily Intakes of Carbohydrates, Proteins, and Water**

GenderAnd Age	Carbohydrates(grams/day)	Proteins(grams/day)	Water*(liters/day)
Males 9–13 years	130	34	2.4
14–18 years	130	52	3.3

Table 4.2: (continued)

GenderAnd Age	Carbohydrates(grams/day)	Proteins(grams/day)	Water*(liters/day)
Females 9–13 years	130	34	2.1
14–18 years	130	46	2.3

- Includes water in foods as well as beverages

Carbohydrates

Carbohydrates are organic (or carbon-containing) compounds consisting of the elements carbon, hydrogen, and oxygen. The elements are arranged in small molecules called saccharides. Carbohydrates are classified as either simple or complex, based on the number of saccharides they contain.

Simple carbohydrates contain just one or two saccharides. They are all sugars. Examples of sugars in the diet include fructose, which is found in fruit, and lactose, which is found in milk. The main function of simple carbohydrates is to provide the body with energy. One gram of carbohydrate provides four kilocalories of energy. Glucose is the sugar that is used most easily by cells for energy. It circulates in the blood, providing energy to cells throughout the body. Glucose is the only source of energy used by the brain.

Complex carbohydrates, called polysaccharides, generally contain many saccharides. They include starches and fiber. Starches are found in plant foods such as vegetables and grains. They are broken down during digestion to form sugars that provide energy. Fiber consists of indigestible starches and other materials such as cellulose. It is present in all plant foods.

Fiber may be soluble or insoluble.

- Soluble fiber dissolves in water as it passes through the large intestine. It helps form substances that keep blood levels of glucose stable and blood levels of harmful lipids low (see below).
- Insoluble fiber does not dissolve but attracts water as it passes through the large intestine. This helps keep waste moist and moving easily through the intestine.

Proteins

Proteins are relatively large organic compounds containing carbon, hydrogen, oxygen, and nitrogen. The elements are arranged in small molecules called amino acids. Amino acids are the building blocks of proteins. They bond together to form long chains, called polypeptides. Proteins consist of one or more polypeptides.

Proteins play many vital roles in the body, including:

- Making up the majority of muscle tissue.
- Regulating many body processes.
- Forming antibodies that destroy bacteria and other ‘‘foreign invaders.”
- Regulating the salt-water and acid-base balance in body fluids.
- Transporting nutrients and other vital substances in the blood.

Dietary proteins are broken down during digestion to provide the amino acids that cells need to make proteins for the body. Twenty different amino acids are needed for this purpose. Ten of these amino acids can be synthesized by cells from simple components. The other ten cannot be synthesized and must be obtained from foods. They are called essential amino acids because they are essential in the diet.

Proteins that contain all ten essential amino acids are referred to as complete proteins. They are found in animal foods such as milk and meat. Proteins that are missing one or more essential amino acids are referred to as incomplete proteins. They are found in plant foods such as legumes and rice. By eating a variety of different plant foods containing incomplete proteins, you can include all ten essential amino acids in your diet.

If you eat more protein than needed for the synthesis of new proteins by cells, the excess is used for energy or stored as fat. One gram of protein provides four kilocalories of energy. This is the same amount of energy that one gram of carbohydrate provides.

Lipids

Lipids, or fatty acids, are organic compounds that consist of repeating units of carbon, hydrogen, and oxygen. They provide the body with energy. The heart and skeletal muscles rely mainly on lipids for fuel. One gram of lipids provides nine kilocalories of energy, more than twice the amount provided by carbohydrates or proteins. Lipids have several other functions as well. Lipids form an insulating sheath around nerve cells that helps nerve messages travel more quickly. Lipids also help form substances that regulate blood pressure, blood clotting, and blood lipid levels. In addition, lipids make up the membranes that surround cells.

The term fat is often used interchangeably with the term lipid, but fats are actually a particular type of lipid, called **triglycerides**, in which three fatty acids are bound to a compound called glycerol. Fats are important in the body. They are the main form in which the body stores energy. Stored body fat is called adipose tissue. Stored fat not only provides an energy reserve but also cushions and protects internal organs. In addition, stored fat insulates the body and helps prevent heat loss in cold weather.

Although lipids and fats are necessary for life, they may be harmful if they are present in the blood at high levels. Both triglycerides and the lipid called cholesterol are known to damage blood vessels if their concentrations in the blood are too high. By damaging blood vessels, triglycerides and cholesterol also increase the risk of heart disease.

Lipids are classified as either saturated fatty acids or unsaturated fatty acids. This classification is based on the number of chemical bonds between carbon atoms in lipid molecules.

- **Saturated fatty acids** have only single bonds between carbon atoms. This gives them properties that make them unhealthful. Their amount in the diet should be kept as low as possible. If consumed in excess, they contribute to high blood levels of cholesterol and triglycerides. Saturated fatty acids are found in animal foods, such as meat, whole milk, and eggs.
- **Unsaturated fatty acids** have at least one double bond between carbon atoms. This gives them properties that make them more healthful. Eaten in appropriate amounts, they may help lower blood levels of cholesterol and triglycerides and decrease the risk of cardiovascular disease. They are found mainly in plant foods.

The human body can synthesize all but two of the fatty acids it needs: omega-3 fatty acids and omega-6 fatty acids. Both are unsaturated fatty acids. They are called essential fatty acids because they must be present in the diet. They are found in salmon, vegetable oil, flaxseed, eggs, and whole grains. Small amounts of these two fatty acids may help lower blood pressure as well as blood levels of harmful lipids.

Unsaturated fatty acids known as trans fatty acids (or trans fats), are manufactured from plant oils and do not occur naturally. They are added to foods to extend their shelf life. Trans fats have properties like saturated fats and may increase risk of cardiovascular disease. They should be avoided in balanced eating. Many manufacturers no longer add trans fats to food products, and their use in restaurants has been banned in some cities.

Water

You may not think of water as a food, but it is a nutrient. Water is essential to life because it is the substance within which all the chemical reactions of life take place. An adult can survive only a few days without water. **Table 1**, above, shows water requirements for young people.

Water is lost from the body in exhaled air, sweat, and urine. Dehydration occurs when a person does not take in enough water to replace the water that is lost. Symptoms of dehydration include headaches, low blood pressure, and dizziness. If dehydration continues, it can quickly lead to unconsciousness and even death. When you are very active, particularly in the heat, you can lose a great deal of water in sweat. To avoid dehydration, you should drink extra fluids before, during, and after exercise.

Taking in too much water—especially without consuming extra salts—can lead to a condition called hyponatremia. In this condition, the brain swells with water, causing symptoms such as nausea, vomiting, headache, and coma. Hyponatremia can be fatal, so it requires emergency medical care.

Balanced Eating

Balanced eating is a way of eating that promotes good health. It includes eating several medium-sized meals regularly throughout the day. It also includes eating the right balance of different foods to provide the body with all the nutrients it needs. **Table 1**, above, lists macronutrient needs for young people, and you just read about foods that provide each of these macronutrients. How much of these foods should you eat to get the right balance of nutrients? Two tools for choosing foods that provide balanced nutrition are MyPyramid and nutrition labels on food packages.

MyPyramid

MyPyramid was developed by the U.S. Food and Drug Administration. It shows how much you should eat each day of foods in different food groups. MyPyramid is shown in **Figure** 4.11. You can visit the MyPyramid.gov website for more details or to customize MyPyramid for your gender, age, activity level, and other factors.

Guidelines for Using MyPyramid

1. The six colored bands represent six food groups:

- Brown = Grains—At least half should be whole grains.
- Green = Vegetables—Choose a variety of vegetables, including dark green and orange vegetables, dry beans and peas.
- Red = Fruits—Include a variety of fruits, and consume whole fruits instead of fruit juices.
- Yellow = Oils—Choose mainly unsaturated nut and vegetable oils.
- Blue = Milk—Dairy products should be low-fat or fat-free choices.
- Purple = Meat and Beans—Choose fish and low-fat meats, as well as beans, peas, nuts, and seeds.

2. The width of each colored band shows the proportion of food that should come from each food group.

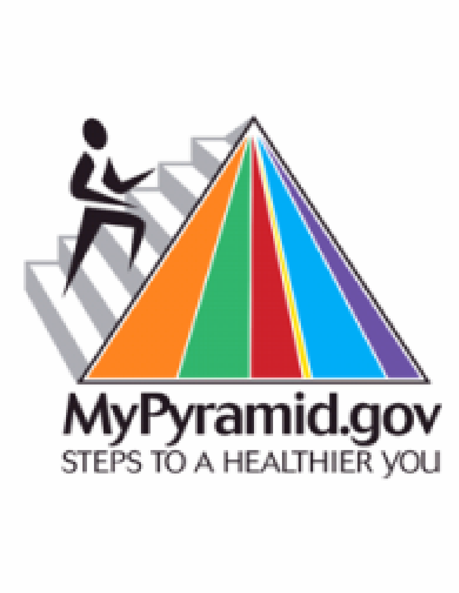

MyPyramid.gov
STEPS TO A HEALTHIER YOU

Figure 4.11: MyPyramid is visual representation of how much you should eat each day of foods in different food groups.

3. The figure climbing stairs reminds you to balance food with exercise: 30–60 min/day of moderate-to-vigorous activity is recommended for most people.

Each food group represented by a colored band in MyPyramid is a good source of nutrients. The wider the band, the more you should eat from that food group. For example, the brown band is widest, so the largest proportion of foods should come from the grains group. The white tip of MyPyramid represents foods that should be eaten only in very small amounts or very infrequently. They include foods such as ice cream and potato chips that contain few nutrients and may contribute excess kilocalories to the diet.

The figure “walking” up the side of MyPyramid in **Figure** 4.11 represents the role of exercise in balanced eating. Daily exercise helps you burn any extra energy that you consume in foods. The more active you are, the more energy you use. Light activities, such as golfing, typically use only a few hundred kilocalories per hour. Strenuous activities, such as running, may use over 900 kilocalories per hour.

Harvard University recently developed an alternative healthy eating pyramid, which is shown in **Figure** 4.12. It differs from MyPyramid in placing more emphasis on exercise and a greater focus on eating fruits, vegetables, and healthy plant oils. It moves red meats and starchy, low-nutrient foods, such as white bread and white rice, to the category of foods to eat in very limited amounts. Some experts think that the Harvard pyramid is less confusing than MyPyramid and represents an even healthier way of eating.

Food Labels

Packaged foods are required by law to carry a nutrition facts label, like the one in **Figure** 4.13, showing the nutrient content and ingredients in the food.

Reading nutrition facts labels can help you choose foods that are high in nutrients such as protein and low in nutrients such as fat. Nutrition facts labels can also help you choose foods that are nutrient dense. Nutrient density is the ratio of nutrient content, measured in grams, to total energy content in kilocalories.

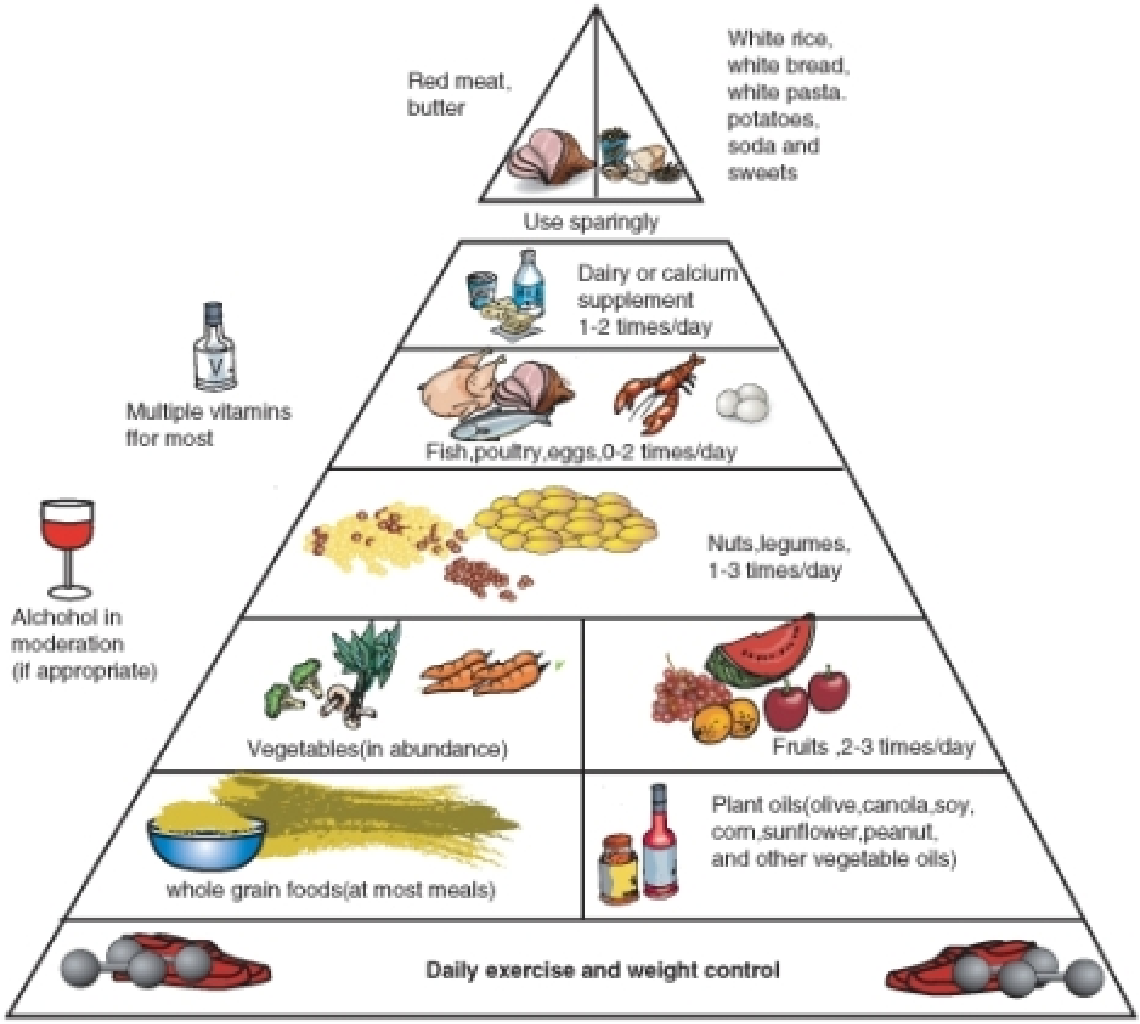
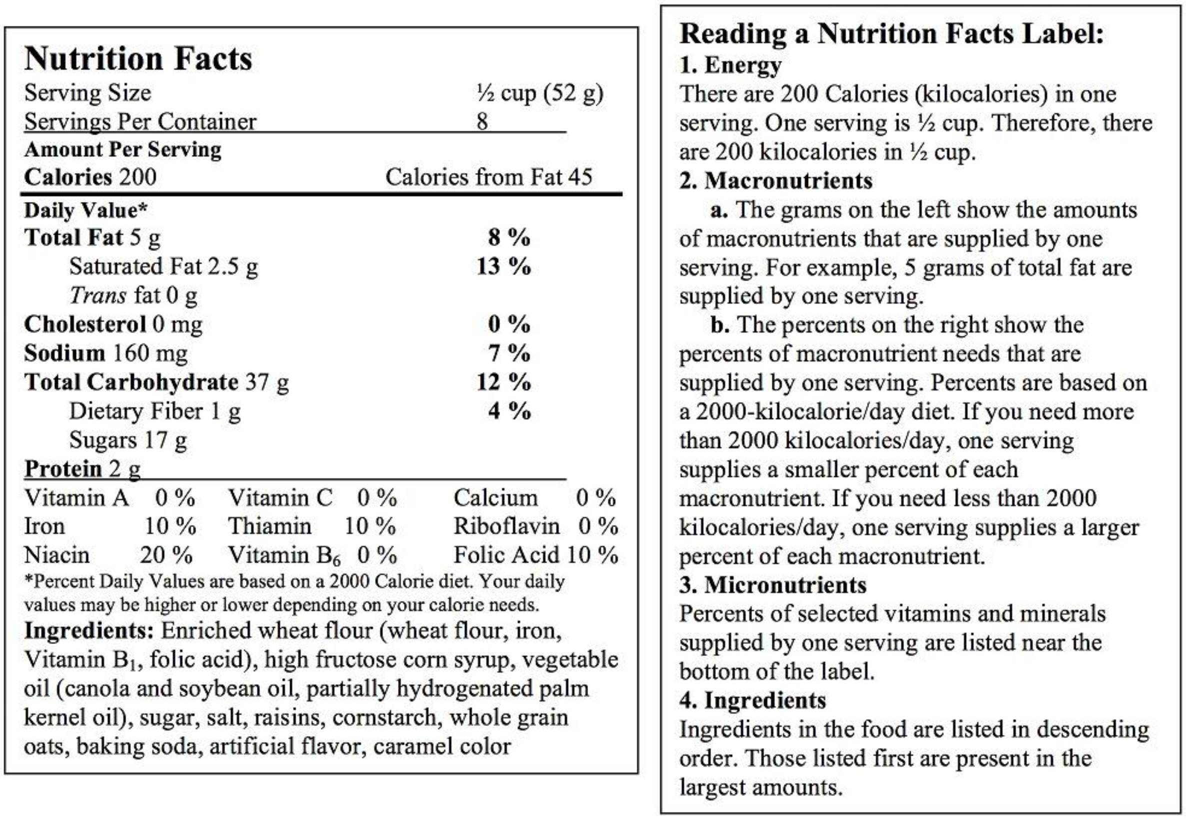

Red meat, butter
White rice, white bread, white pasta, potatoes, soda and sweets
Use sparingly
Dairy or calcium supplement 1-2 times/day
Multiple vitamins ffor most
Fish,poultry,eggs,0-2 times/day
Nuts,legumes, 1-3 times/day
Alchohol in moderation (if appropriate)
Vegetables(in abundance)
Fruits ,2-3 times/day
whole grain foods(at most meals)
Plant oils(olive,canola,soy, corn,sunflower,peanut, and other vegetable oils)
Daily exercise and weight control

Figure 4.12: Healthy eating pyramid.



Nutrition Facts

Serving Size	½ cup (52 g)
Servings Per Container	8
Amount Per Serving	
Calories 200	Calories from Fat 45
Daily Value*	
Total Fat 5 g	**8 %**
Saturated Fat 2.5 g	**13 %**
Trans fat 0 g	
Cholesterol 0 mg	**0 %**
Sodium 160 mg	**7 %**
Total Carbohydrate 37 g	**12 %**
Dietary Fiber 1 g	**4 %**
Sugars 17 g	
Protein 2 g	

Vitamin A	0 %	Vitamin C	0 %	Calcium	0 %
Iron	10 %	Thiamin	10 %	Riboflavin	0 %
Niacin	20 %	Vitamin B_6	0 %	Folic Acid	10 %

*Percent Daily Values are based on a 2000 Calorie diet. Your daily values may be higher or lower depending on your calorie needs.

Ingredients: Enriched wheat flour (wheat flour, iron, Vitamin B_1, folic acid), high fructose corn syrup, vegetable oil (canola and soybean oil, partially hydrogenated palm kernel oil), sugar, salt, raisins, cornstarch, whole grain oats, baking soda, artificial flavor, caramel color

Reading a Nutrition Facts Label:

1. Energy

There are 200 Calories (kilocalories) in one serving. One serving is ½ cup. Therefore, there are 200 kilocalories in ½ cup.

2. Macronutrients

a. The grams on the left show the amounts of macronutrients that are supplied by one serving. For example, 5 grams of total fat are supplied by one serving.

b. The percents on the right show the percents of macronutrient needs that are supplied by one serving. Percents are based on a 2000-kilocalorie/day diet. If you need more than 2000 kilocalories/day, one serving supplies a smaller percent of each macronutrient. If you need less than 2000 kilocalories/day, one serving supplies a larger percent of each macronutrient.

3. Micronutrients

Percents of selected vitamins and minerals supplied by one serving are listed near the bottom of the label.

4. Ingredients

Ingredients in the food are listed in descending order. Those listed first are present in the largest amounts.

Figure 4.13: Nutrition facts label.

Table 4.3: **Consider the following two foods:**

15g/300 kcal = 0.05 g/kcal	10g/120 kcal = 0.08 g/kcal
Nutrient Density:	Nutrient Density:
Energy: 300 kcal	Energy: 120 kcal
Protein: 15 g	Protein: 10 g
Food A	**Food B**

In terms of protein, Food B is more nutrient dense than Food A, because it provides more protein per kilocalorie. Eating nutrient-dense foods helps you to get enough of each nutrient without taking in too many kilocalories.

Reading the ingredients list on food labels can also help you choose healthful foods for balanced eating. At the top of the list, look for ingredients such as whole grains, vegetables, and fruits. These are foods you need the most of in a balanced diet. Avoid foods that contain processed ingredients, such as white flour or white rice. Processing removes nutrients. As a result, processed foods generally supply fewer nutrients than whole foods, even when they have been enriched or fortified with added nutrients.

Weight Gain and Obesity

Any unneeded energy in food, whether it comes from carbohydrates, proteins, or lipids, is stored in the body as fat. An extra 3,500 kilocalories of energy results in the storage of one pound (0.45 kg) of fat. People who consistently consume more food energy then they need gain weight. People who continue to store fat and gain weight may eventually become obese.

Obesity occurs when the body mass index is 30.0 kg/m_2 or greater. Body mass index (BMI) is a simple way to estimate the percentage of fat in the body. It is calculated by dividing an individual's weight (in kilograms) by the square of the individual's height (in meters). For example, a man who weighs 88 kilograms and is 1.7 meters tall has a BMI of:

$88\text{ kg} \div (1.7\text{ m})^2 = 30.4\text{ kg/m}^2$.

Compare this BMI with the BMI values in **Table** 4.4. The man's BMI is greater than 29.9 kg/m^2, so he would be considered obese.

Table 4.4: **Body Mass Index and Weight Status**

BMI Value (kg/m^2)	Weight Status
<18.5	Underweight
18.5–24.9	Normal weight
25.0–29.9	Overweight
>29.9	Obese

People who are obese are at greater risk of many serious health problems, including metabolic syndrome. **Metabolic syndrome** is a cluster of conditions that together greatly increase the risk of cardiovascular disease. The conditions include type 2 diabetes, high blood pressure, and high blood levels of LDL cholesterol and triglycerides. A wide range of other disorders may also be related to obesity, including menstrual disorders in females, certain types of cancer, osteoarthritis, and depression. In addition, people who are obese have a lower life expectancy.

From 1980 to 2002, the number of obese adults in the U.S. doubled. By 2004, almost one-third of U.S. adults aged 20 years or older were obese. The prevalence of obesity in the U.S. is the highest in the developed world. Given its prevalence and serious health risks, obesity is now a leading public health problem in this country.

The combination of eating too much and moving too little generally causes obesity. The best way to lose weight and avoid obesity is to eat less and exercise more. However, many factors may play a role in obesity, making it difficult for most people to eat wisely and lose weight. These factors may be genetic or environmental.

Several genes have been identified that control appetite and may contribute to some cases of obesity. An important environmental factor that contributes to obesity is the availability of high-fat, high-Calorie fast foods. Other environmental factors that may influence eating habits and contribute to obesity include stress, cultural traditions, and food advertisements. Some people who are obese have an eating disorder called binge eating. Eating disorders are discussed below.

Vitamins and Minerals

Unlike the major macronutrients, micronutrients—including vitamins and minerals—do not provide energy. Nonetheless, adequate amounts of micronutrients are essential for good health. The needed amounts generally can be met with balanced eating. However, many people do not eat enough of the right foods to meet their requirements. They may need vitamin or mineral supplements to increase their intake of micronutrients.

Vitamins

Vitamins are organic compounds that are needed by the body to function properly. There are 13 vitamins that humans need. They are described in **Table** 4.5, which also includes recommended daily vitamin intakes for teens.

Vitamins play many roles in good health, ranging from helping maintain vision to helping form red blood cells. Many vitamins are components of enzymes. For example, vitamin K is a component of enzymes involved in blood clotting. Several vitamins, including vitamins C and E, act as antioxidants. An antioxidant is a compound that neutralizes chemicals called free radicals. Free radicals are produced naturally during cellular activities and may cause some types of cancer. Neutralizing free radicals makes them harmless.

Some vitamins, including vitamin B_6, are produced by bacteria that normally live in the intestines, where they help digest food. Vitamin D is synthesized in the skin when it is exposed to UV radiation in sunlight. Most other vitamins must be obtained from foods because the body is unable to synthesize them. Good food sources of vitamins are listed in the table below. They include whole grains, vegetables, fruits, milk, and nuts.

Consuming inadequate amounts of vitamins can cause deficiency diseases. For example, consuming inadequate amounts of vitamin D causes soft bones. In children this is called rickets. It can cause permanent bone deformities. Consuming too much of some vitamins can also be dangerous. Overdoses of vitamins can cause problems ranging from diarrhea to birth defects and even death.

Vitamins are either fat-soluble or water-soluble. This determines whether they can accumulate in the body and lead to overdoses.

- Vitamins A, D, E, and K are fat soluble. Excess intakes of these vitamins are stored in fatty tissues of the body. Because they are stored in the body, they can build up to toxic levels, especially if they are taken improperly in supplements.
- Vitamin C and all the B vitamins are water soluble. Excess amounts of these vitamins are excreted in the urine, so they are unlikely to reach toxic levels in the body.

Table 4.5: **Vitamins**

Vitamin (Chemical Name)	Functions in the Body	Good Food Sources	Recommended Daily Intakes f or Ages 14–18 yr
(Retinoids) Vitamin A	Needed for good vision, reproduction, and fetal development	Carrots, spinach, milk, eggs	Females: 700 μg Males: 900 μg
(Thiamine) Vitamin B_1	Helps break down macronutrients; essential for proper functioning of nerves	Whole wheat, peas, beans, fish, peanuts, meats	Females: 1.0 mg Males: 1.2 mg
(Riboflavin) Vitamin B_2	Helps the body process amino acids and fats; acts as antioxidant	Milk, liver, green leafy vegetables, almonds, soybeans	Females: 1.0 mg Males: 1.3 mg
(Niacin) Vitamin B_3	Helps release energy from macronutrients; needed for healthy skin and nerves	Beets, beef liver, pork, turkey, fish, sunflower seeds, peanuts	Females: 14 mg Males: 16 mg
(Pantothenic Acid) Vitamin B_5,	Helps form critical enzymes for synthesis of macronutrients	Whole grains, legumes, eggs, meat	Females: 5mg* Males: 5 mg*
(Pyridoxine) Vitamin B_6	Forms enzymes needed for amino acid synthesis and energy storage	Cereals, yeast, liver, fish, avocadoes, nuts, green beans	Females: 1.2 mg Males: 1.3 mg
(Biotin) Vitamin B_7	Enables synthesis of fatty acids; helps store energy; keeps level of blood sugar stable	None	Females: 25 μg* Males: 25 μg*
(Folate) Vitamin B_9	Needed to make red blood cells	Liver, green leafy vegetables, dried beans and peas	Females: 400 μg Males: 400 μg

Table 4.5: (continued)

Vitamin (Chemical Name)	Functions in the Body	Good Food Sources	Recommended Daily Intakes f or Ages 14–18 yr
(Cyanocobalamin) Vitamin B_{12}	Needed for normal functioning of nervous system and formation of blood	Meat, liver, milk, shellfish, eggs	Females: 2.4 μg Males: 2.4 μg
(Ascorbic Acid) Vitamin C	Needed to make many biological chemicals; acts as antioxidant	Citrus fruits such as oranges, red peppers, broccoli, kiwi	Females: 65 mg Males: 75 mg
(Ergocalciferol and Cholecalciferol) Vitamin D	Helps maintain blood levels of calcium; needed for healthy bones and teeth	Salmon, tuna, eggs, mushrooms	Females: 5 μg Males: 5 μg
(Tocopherol) Vitamin E	Acts as antioxidant; protects cell membranes from LDL cholesterol damage	Vegetable oils, nuts, green leafy vegetables, whole grains, fish	Females: 15 mg Males: 15 mg
(Naphthoquinone) Vitamin K	Helps transport calcium; helps blood clot	Kale, spinach, Brussels sprouts, milk, eggs, soy products	Females: 75 μg* Males: 75 μg*

- Recommended daily intakes not established; figures given are adequate daily intakes.

Minerals

Dietary minerals are chemical elements that are essential for body processes. Minerals are inorganic, meaning they do not contain carbon. Minerals needed by humans in relatively large amounts (greater than 200 mg/day) are listed in **Table** 4.6. Minerals not listed in the table are called trace minerals because they are needed in very small amounts. Trace minerals include chromium, iodine, iron, molybdenum, selenium, and zinc.

Table 4.6: **Minerals**

Mineral Name (Symbol)	Functions in the Body	Good Food Sources	Recommended Daily Intakes (mg) for Ages 14–18 yr
(Ca) Calcium	Needed for nerve and muscle action; builds bone and teeth; helps blood clot	Milk, soy milk, green leafy vegetables, sardines	Females: 1300* Males: 1300*

Table 4.6: (continued)

Mineral Name (Symbol)	Functions in the Body	Good Food Sources	Recommended Daily Intakes (mg) for Ages 14–18 yr
(Cl) Chloride	Helps maintain water and pH balance; helps form stomach acid	Table salt, most processed foods	Females: 2300* Males: 2300*
(Mg) Magnesium	Needed to form several enzymes	Whole grains, green leafy vegetables, nuts, seeds	Females: 360 Males: 410
(P) Phosphorus	Component of bones, teeth, lipids, and other important molecules in the body	Meat, poultry, whole grains	Females: 1250 Males: 1250
(K) Potassium	Needed for muscle and nerve function; helps maintain salt-water balance in body fluids	Meats, grains, orange juice, potatoes, bananas	Females: 4700* Males: 4700*
(Na) Sodium	Needed for muscle and nerve function; helps maintain salt-water balance in body fluids	Table salt, most processed foods	Females: 1500* Males: 1500*
(S) Sulfur	Necessary component of many proteins	Whole grains, meats, seafood, eggs	Females: 1300* Males: 1300*

- Recommended daily intakes not established; figures given are adequate daily intakes.

Minerals play many important roles in the body. Most are found in the blood and cytoplasm of cells, where they control basic functions. For example, calcium and potassium regulate nerve and muscle activity. Several minerals, including zinc, are components of enzymes. Other minerals, including calcium, form the bulk of teeth and bones.

Minerals cannot be synthesized by the body. Good food sources of minerals are listed in **Table** 4.6. They include dairy products, green leafy vegetables, and legumes. Mineral deficiencies are uncommon, but inadequate intakes of a few minerals may lead to health problems. For example, an inadequate intake of calcium may contribute to osteoporosis, a disease in which bones become brittle and break easily.

Some minerals may be toxic in excess, but overdoses of most minerals are uncommon. Overdoses are more likely when mineral supplements are taken. Salt (sodium chloride) is added to many foods, so the intake of sodium may be too high in many people. Too much sodium in the diet can cause high blood pressure in some individuals.

Other Micronutrients

Recently, new micronutrients called phytochemicals have been found in plants. They occur primarily in colorful fruits and vegetables, like those shown in **Figure** 4.14. Thousands of phytochemicals have been discovered, and some have already been shown to lower the risk of certain diseases. For example, the phytochemical lutein helps reduce the risk of macular degeneration, an eye disease that leads to blindness. Lutein is found in many yellow and orange fruits and vegetables. Several phytochemicals, including some found in berries, have proven to be powerful antioxidants.

Figure 4.14: Good sources of phytochemicals.

Eating Disorders

Eating disorders are psychiatric illnesses that involve abnormal patterns of eating. A person with an eating disorder has a compulsion to eat in a way that causes physical, mental, and emotional health problems. Typically, the person has an obsession with food and weight. Eating disorders are more common in females. One reason may be society's focus on female appearance. The most common eating disorders are binge eating disorder, anorexia nervosa, and bulimia nervosa.

Binge Eating Disorder

Binge eating disorder is characterized by compulsive overeating. People with the disorder typically eat very large quantities of food in a short period of time. They may use food as a way to deal with painful emotions or stress. Many people with the disorder are overweight or obese. The disorder is rapidly increasing in prevalence and is now the most common eating disorder in the U.S. The rise in binge eating disorder is one reason for the dramatic increase in obesity in this country

Anorexia Nervosa

Anorexia nervosa is characterized by greatly restricted food intake and low body weight (BMI less than 17.5 kg/m^2). People with anorexia nervosa usually have a distorted body image. They think they are too fat when they are actually too thin. They have an obsessive fear of gaining weight and voluntarily starve themselves. They may also exercise excessively to help keep their weight low. Females with anorexia nervosa usually stop having menstrual periods. The disorder mainly affects teenage girls and is extremely serious. At least 10 percent of people with anorexia nervosa die from factors related to the disorder.

Bulimia Nervosa

Bulimia nervosa is characterized by cycles of binge eating followed by purging to eliminate the food from the body. Purging may be achieved through intentional vomiting or excessive use of laxatives. People with this disorder typically have normal weight or weight slightly greater than normal. Repeated purging can lead to dehydration. Excessive vomiting can damage the teeth and organs of the digestive system. Bulimia nervosa occurs most often in teenage girls and young women.

Causes and Treatment

People with eating disorders usually have other mental health problems as well, most commonly depression. Both depression and eating disorders may have the same underlying physiological cause: low levels of the brain chemical serotonin. The process of eating causes serotonin to be released and may lead to a temporary "high." The process of purging may also have this effect in people with bulimia nervosa.

Environmental factors play a role in most cases of eating disorders, as they do with depression and other mental health problems. Childhood abuse may be one of these environmental factors. Many people with eating disorders report having been abused as children.

Eating disorders can be treated with psychiatric therapy or psychological counseling. Medications may also be prescribed. Treatment usually includes resolving underlying emotional problems, as well as treating depression or other mental health disorders that are also present. In patients with anorexia nervosa, weight gain is also an important goal of treatment.

Lesson Summary

- Macronutrients include carbohydrates, proteins, and lipids. They are needed in relatively large amounts to supply the body with energy and building materials.
- Balanced eating can provide the body with the nutrients it needs without causing weight gain. Balanced eating includes eating a wide variety of healthful foods.
- Vitamins and minerals are micronutrients. They are needed in relatively small amounts to control many body processes.
- Eating disorders are serious but treatable psychiatric illnesses. They involve abnormal eating patterns and an obsession with food and weight.

Review Questions

1. Which classes of nutrients provide the body with energy?
2. How is obesity diagnosed?
3. Identify the two main classes of micronutrients and give an example of each.
4. What is an eating disorder?
5. If Jera is a 15-year-old female, how many grams of carbohydrates and proteins should she eat each day?
6. How can MyPyramid help you have a balanced diet?
7. Why is it more dangerous to consume too much of a fat-soluble vitamin than a water-soluble vitamin?

8. Compare and contrast anorexia nervosa and bulimia nervosa.

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Vocabulary

anorexia nervosa Eating disorder characterized by greatly restricted food intake and low body weight.

bulimia nervosa Eating disorder characterized by cycles of binge eating followed by purging to eliminate the food from the body.

binge eating disorder Eating disorder characterized by compulsive overeating. People with the disorder typically eat very large quantities of food in a short period of time.

carbohydrates Organic (or carbon-containing) compounds consisting of the elements carbon, hydrogen, and oxygen; provides the body with energy.

complete proteins Contain all ten essential amino acids; found in animal foods such as milk and meat.

eating disorder Psychiatric illnesses that involve abnormal patterns of eating.

essential amino acids Amino acids that cannot be synthesized and must be obtained from the diet.

hyponatremia A condition in which the brain swells with water, causing symptoms such as nausea, vomiting, headache, and coma.

incomplete proteins Proteins that are missing one or more essential amino acids; found in plant foods such as legumes and rice.

lipids (fatty acids) Organic compounds that consist of repeating units of carbon, hydrogen, and oxygen; provide the body with energy.

macronutrients Nutrients that the body needs in relatively large amounts; include carbohydrates, proteins, lipids, and water.

metabolic syndrome A cluster of conditions that together greatly increase the risk of cardiovascular disease; include type 2 diabetes, high blood pressure, and high blood levels of LDL cholesterol and triglycerides.

micronutrients Nutrients the body needs in relatively small amounts; include vitamins and minerals.

minerals Inorganic chemical elements that are essential for body processes.

MyPyramid A visual representation of how much you should eat each day of foods in different food groups.

nutrients Chemical elements or compounds that the body needs for normal functioning and good health.

obesity Occurs when the body mass index is 30.0 kg/m_2 or greater.

proteins Relatively large organic compounds containing carbon, hydrogen, oxygen, and nitrogen; made of amino acids.

saturated fatty acids Fatty acids with only single bonds between carbon atoms.

triglyceride Fat; a particular type of lipid in which three fatty acids are bound to a compound called glycerol.

unsaturated fatty acids Fatty acids with at least one double bond between carbon atoms.

vitamins Organic compounds that are needed by the body to function properly. There are 13 vitamins that humans need.

Points to Consider

- You need nutrients for energy and building materials. Balanced eating provides you with foods that contain the nutrients you need. How does your body obtain the nutrients from food?
- What processes break down food and make nutrients available to the body? What organs carry out the processes?

Chapter 5

Immune System and Disease

5.1 Immune System: The Nonspecific Defenses

Lesson Objectives

- Describe mechanical, chemical, and biological barriers that keep most pathogens out of the human body.
- Explain how the inflammatory response and white blood cells help fight pathogens that enter the body.

Introduction

(Overview of the immune reponse from the Nobel Prize organization: http://nobelprize.org/educational/medicine/imm
overview.html)

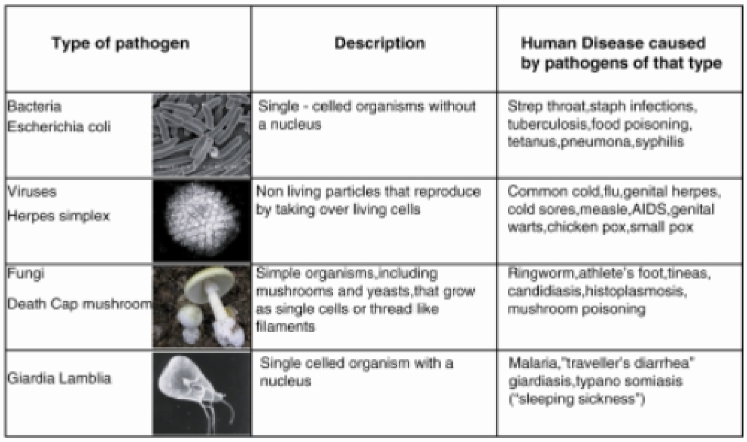
The immune system protects the body from "germs" and other harmful substances. The immune system is like a medieval castle. The outside of a medieval castle was protected by a moat and high stone walls. Inside the castle, soldiers were ready to defend the castle against any invaders that got through the outer defenses. Like a medieval castle, the immune system has a series of defenses. Only pathogens that are able to get through all the defenses can cause harm to the body.

First Line of Defense

The immune system has three lines of defense. The first line of defense includes a variety of barriers against pathogens that keep most pathogens out of the body. Pathogens are disease-causing agents, such as bacteria and viruses. Defenses in the first line are the same regardless of the type of pathogen. This is why they are called nonspecific defenses. Several types of pathogens that are common causes of human disease can be seen in the **Figure** 5.1.

Mechanical Barriers

Mechanical barriers physically block pathogens from entering the body. The skin is the most important mechanical barrier. In fact, it is the single most important defense of the body against pathogens. It forms



Type of pathogen	Description	Human Disease caused by pathogens of that type
Bacteria Escherichia coli	Single - celled organisms without a nucleus	Strep throat,staph infections, tuberculosis,food poisoning, tetanus,pneumona,syphilis
Viruses Herpes simplex	Non living particles that reproduce by taking over living cells	Common cold,flu,genital herpes, cold sores,measle,AIDS,genital warts,chicken pox,small pox
Fungi Death Cap mushroom	Simple organisms,including mushrooms and yeasts,that grow as single cells or thread like filaments	Ringworm,athlete's foot,tineas, candidiasis,histoplasmosis, mushroom poisoning
Giardia Lamblia	Single celled organism with a nucleus	Malaria,"traveller's diarrhea" giardiasis,typano somiasis ("sleeping sickness")

Figure 5.1: Common Human Pathogens

a physical barrier between the body and the outside world. The outer layer of the skin is a tough, nearly water-proof coating that is very difficult for pathogens to penetrate.

At body openings, such as the mouth and nose, the body has a different mechanical barrier. Instead of skin, mucous membranes line these and other organs that are exposed to the outside environment. They include the organs of the respiratory, gastrointestinal, and urinary tracts. Mucous membranes secrete mucus, a slimy substance that coats the membranes and traps pathogens. Mucous membranes also have cilia, which are tiny projections that have wavelike motions. The movements of cilia sweep mucus and trapped pathogens toward body openings to be removed from the body.

Pathogens are removed from the respiratory tract when you sneeze or cough. In addition, tears wash pathogens from the eyes, and urine flushes pathogens out of the urinary tract.

Chemical Barriers

Chemical barriers are proteins that destroy pathogens at the body's surface. The skin and mucous membranes secrete proteins that kill many of the pathogens with which they come into contact. For example, enzymes called lysozymes—which are found in sweat, mucus, tears, and saliva—kill pathogens by breaking open their cell walls. Urine and vaginal secretions are too acidic for many pathogens, and semen contains zinc, which most pathogens cannot tolerate. Hydrochloric acid secreted by mucous membranes lining the stomach kills pathogens that enter the stomach in food or water.

Biological Barriers

Biological barriers involve living organisms that compete with pathogens. Human skin is covered by millions of bacteria. Millions more colonize the gastrointestinal, urinary, and genital tracts. Most of these bacteria are helpful or at least not harmful. They are important in defense because they help prevent harmful bacteria from becoming established in or on the body. They do this by competing with harmful bacterial for food and space. Helpful bacteria may also change pH or other factors and make conditions less suitable for harmful bacteria.

Second Line of Defense

If you have a cut on your hand, the break in the skin provides a way for pathogens to enter your body. Assume bacteria enter through the cut and infect the wound. These bacteria would then encounter the second line of defense.

Inflammatory Response (http://www.sumanasinc.com/webcontent/animations/

The cut on your hand is likely to become red, warm, swollen, and painful. These are all signs that an inflammatory response has occurred. An inflammatory response is a complex biological reaction to tissue damage. It is one of the first responses of the immune system to infection or injury. Inflammation is triggered by chemicals called cytokines and histamines, which are released when tissues are damaged.

- Cytokines are chemical signals used to communicate between cells.
- Histamines are chemicals that cause inflammation and allergies.

The cytokines and histamines released when tissue is damaged cause many changes in the damaged tissue. The changes help remove the cause of the damage and start the healing process. For example, the chemicals cause local blood vessels to dilate, which increases blood flow to the area. They also cause other changes in blood vessels that allow blood components to leak into the damaged tissue.

White Blood Cells

Another role of cytokines is to attract white blood cells, or leukocytes, to the site of inflammation. Leukocytes are immune system cells that are specialized to fight infections. They are the primary cells of the immune system and found throughout the body. The general function of leukocytes is to identify and eliminate pathogens, debris, and abnormal body cells. **Figure** 5.2 shows several different types of leukocytes. Each type plays a different role in the removal of pathogens and other unwanted substances from the body.

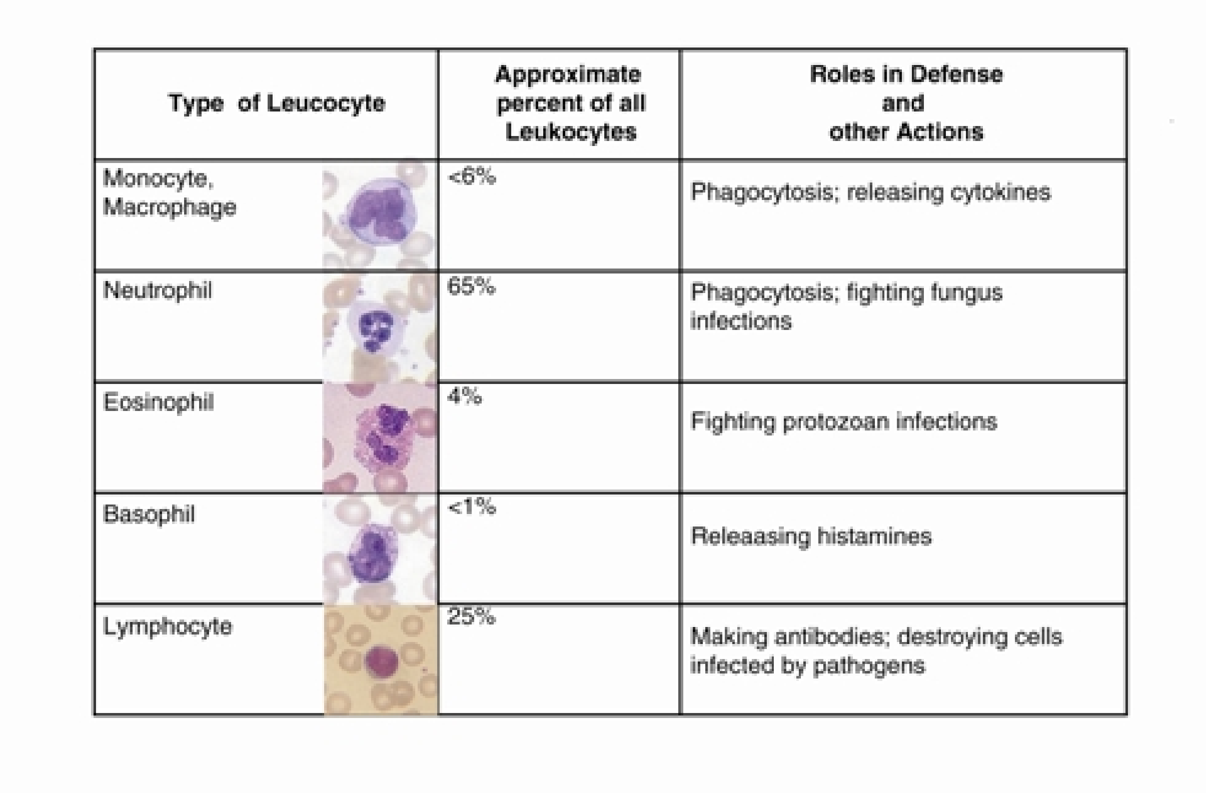
Some leukocytes are nonspecific and respond in the same way to most pathogens. Nonspecific leukocytes include monocytes, macrophages, neutrophils, eosinophils, and basophils. These leukocytes are part of the second line of defense. A magnified image of an actual macrophage is shown in **Figure** 5.3.

Monocytes, macrophages, and neutrophils destroy pathogens in the blood and tissues by phagocytosis. Phagocytosis is the process of engulfing and breaking down pathogens and other unwanted substances. Phagocytosis of a pathogen by a macrophage is illustrated in **Figure** 5.4. Once a pathogen has been engulfed, it is broken down within the macrophage. Macrophages are found in tissues, and monocytes and neutrophils are found in the blood.

Both monocytes and neutrophils migrate through the bloodstream to sites of inflammation. Neutrophils are the most common leukocytes and usually the first leukocytes to arrive at the scene of infection. Neutrophils and dead pathogens are the main components of pus.

In addition to phagocytosis, both monocytes and phagocytes produce chemicals such as cytokines that cause inflammation and fever. A fever is a higher-than-normal body temperature that may help fight infection. Monocytes or macrophages may also trigger the third line of defense, which you will read about in Lesson 24.2: Immune Response.

Eosinophils and basophils are responsible for allergies, which are discussed in Lesson 24.3: Immune System Diseases. Eosinophils also help fight infections by combating parasites such as protozoa. Basophils release cytokines, histamines, and other chemicals that contribute to inflammation as well as allergies.



Type of Leucocyte	Approximate percent of all Leukocytes	Roles in Defense and other Actions
Monocyte, Macrophage	<6%	Phagocytosis; releasing cytokines
Neutrophil	65%	Phagocytosis; fighting fungus infections
Eosinophil	4%	Fighting protozoan infections
Basophil	<1%	Releaasing histamines
Lymphocyte	25%	Making antibodies; destroying cells infected by pathogens

Figure 5.2: Types of Leukocytes

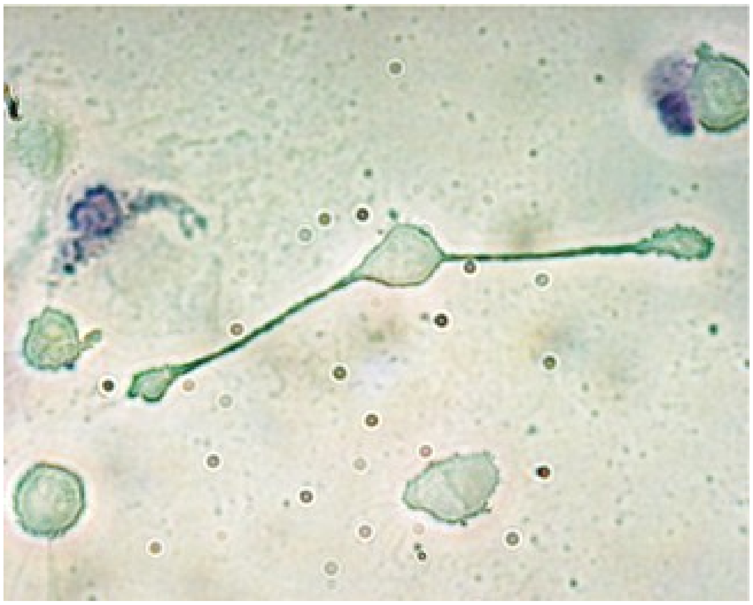


Figure 5.3: Magnified image of a macrophage.

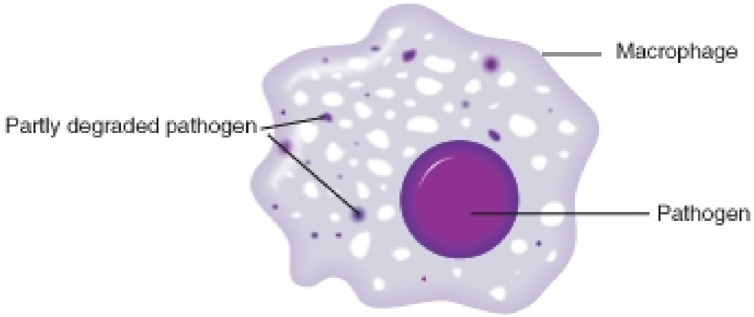


Figure 5.4: Phagocytosis by a macrophage.

Lymphocytes are different from these nonspecific leukocytes. Lymphocytes launch an attack that is tailored to a particular pathogen. For example, some lymphocytes attack only herpes viruses, others only flu viruses. This is called a specific defense. This type of defense is the topic of the next lesson.

Lesson Summary

- Mechanical, chemical, and biological barriers are the body's first line of defense against pathogens.
- The inflammatory response and phagocytosis by white blood cells are major components of the body's second line of defense.

Review Questions

1. Identify two defenses in the body's first line of defense.
2. Describe the process of phagocytosis.
3. How does the inflammatory response help fight infections?
4. Describe the roles of leukocytes in the body's second line of defense.

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Vocabulary

biological barriers Living organisms that compete with pathogens; help prevent harmful bacteria from becoming established in or on the body.

chemical barriers Proteins that destroy pathogens at the body's surface.

cytokines Chemical signals used to communicate between cells.

fever A higher-than-normal body temperature that may help fight infection.

histamines Chemicals that cause inflammation and allergies.

inflammatory response A complex biological reaction to tissue damage; one of the first responses of the immune system to infection or injury; triggered by chemicals called cytokines and histamines.

lysozymes Enzymes that kill pathogens by breaking open their cell walls; found in sweat, mucus, tears, and saliva.

mechanical barriers Physically blocks pathogens from entering the body; the skin is the most important mechanical barrier.

mucus A slimy substance secreted by mucus membranes; coats the membranes and traps pathogens.

nonspecific defenses Defenses that are the same regardless of the type of pathogen; found in the first and second line of defense.

pathogens Disease-causing agents, such as bacteria and viruses.

phagocytosis The process of engulfing and breaking down pathogens and other unwanted substances.

white blood cells Leukocytes; immune system cells that are specialized to fight infections; they identify and eliminate pathogens, debris, and abnormal body cells; leukocytes includes monocytes, macrophages, neutrophils, eosinophils, and basophils.

Points to Consider

The body's first and second lines of defense are the same regardless of the particular pathogen involved. The body's third line of defense is different. It defends the body against specific pathogens.

- Think about how the immune system could identify a particular pathogen.
- Can you develop possible mechanisms for how these pathogens could be destroyed?
- What roles do you think various cell types (such as lymphocytes) play in the specific defenses of the immune system?

5.2 Specific Immune Response

(overview: http://www.biology.arizona.edu/immunology/tutorials/immunology

Lesson Objectives

- Describe the lymphatic system and state its general functions in the immune response.
- Explain the role of antigens in the immune response.
- List the steps that occur in a humoral immune response.
- Identify roles of different types of T cells in a cell-mediated immune response.
- Define immunity and distinguish between active and passive immunity.

Introduction

If pathogens manage to get through the body's first two lines of defense, a third line of defense takes over. This third line of defense is often referred to as the immune response. This defense is specific to a particular pathogen, and it allows the immune system to "remember" the pathogen after the infection is over. If the pathogen tries to invade the body again, the immune system can launch a much faster, stronger attack. This lets the immune system destroy the pathogen before it can cause harm. The immune response mainly involves the lymphatic system.

Lymphatic System

The lymphatic system is a major component of the immune system. Because of its important role in the immune system, the terms "immune system" and "lymphatic system" are sometimes used interchangeably. However, as you read in Lesson 24.1, nonspecific defenses of the body include organs such as the skin, which is not part of the lymphatic system. In addition, the lymphatic system has another function not directly related to defense.

Functions of the Lymphatic System

The lymphatic system has three basic functions. The first function is related to digestion. The other functions are involved in the immune response.

1. The lymphatic system absorbs fatty acids after the digestion of lipids in the small intestine. It then transports the fatty acids to the bloodstream, where they circulate throughout the body.
2. The lymphatic system removes excess fluid from body tissues and returns the fluid to the blood. The fluid is filtered as it passes through the lymphatic system, and any pathogens it contains are destroyed before the fluid enters the bloodstream.
3. The lymphatic system produces lymphocytes. Lymphocytes are the type of white blood cells, or leukocytes, primarily involved in the immune response. They recognize and help destroy specific foreign invaders in body fluids and cells.

Parts of the Lymphatic System

The lymphatic system, which is shown in **Figure** 5.5, consists of lymphatic organs, lymphatic vessels, lymph, and lymph nodes. Organs of the lymphatic system include the red bone marrow, thymus, spleen, and tonsils.

- Red bone marrow is found inside many bones, including the hip, breast, and skull bones. It produces leukocytes.
- The thymus is a gland located in the upper chest behind the breast bone. It stores and matures lymphocytes.
- The spleen is a gland in the upper abdomen. It filters blood and destroys worn-out red blood cells. Lymphocytes in the spleen destroy any pathogens filtered out of the blood.
- Tonsils are glands on either side of the pharynx in the throat. They trap pathogens, which are then destroyed by lymphocytes in the tonsils.

Lymphatic vessels make up a body-wide circulatory system, similar to the arteries and veins of the cardiovascular system. However, lymphatic vessels circulate lymph instead of blood. Lymph is fluid that leaks out of tiny blood vessels, called capillaries, into spaces between cells in tissues. At sites of inflammation, there is usually more lymph around cells, and it is likely to contain many pathogens.

Unlike the cardiovascular system, the lymphatic system does not have a pump to force lymph through its vessels. Lymph circulates due to peristalsis of lymphatic vessels and rhythmic contractions of the skeletal muscles that surround the vessels. Valves in the lymphatic vessels prevent lymph from flowing backwards through the system.

As lymph accumulates between cells, it diffuses into tiny lymphatic vessels. The lymph then moves through the lymphatic system, from smaller to larger vessels, until it reaches the main lymphatic ducts in the chest. Here, the lymph drains into the bloodstream.

Before lymph reaches the bloodstream, pathogens are filtered out of it at lymph nodes. Lymph nodes are small, oval structures located along the lymphatic vessels that act like filters. Any pathogens filtered out of the lymph at lymph nodes are destroyed by lymphocytes in the nodes.

Lymphocytes

Lymphocytes are the key cells involved in the immune response. There are an estimated two trillion lymphocytes in the human body, and they make up about 25 percent of all leukocytes. Usually, fewer than half the body's lymphocytes are found in the blood. The rest are found in the lymphatic system, where they are most likely to encounter pathogens.

The immune response depends on two types of lymphocytes: B lymphocytes, or B cells, and T lymphocytes, or T cells. Both types of lymphocytes are produced in the red bone marrow. The two types are named for the sites where they mature. B cells mature in the red bone marrow, and T cells mature in the thymus. Both B and T cells can recognize and respond to specific pathogens. B or T cells that respond to the body's own molecules as though they were foreign, or ‘‘nonself,’’ receive a signal that causes them to die. Only those B and T cells that have shown they are unlikely to react to ‘‘self’’ molecules are released into the circulation.

Antigen Recognition

B and T cells do not actually recognize and respond to pathogens but to the antigens they carry. Antigens are protein molecules that the immune system recognizes as nonself. Any protein that can trigger an immune response because it is foreign to the body is called an antigen. Antigens include proteins on pathogens, cancer cells, and the cells of transplanted organs.

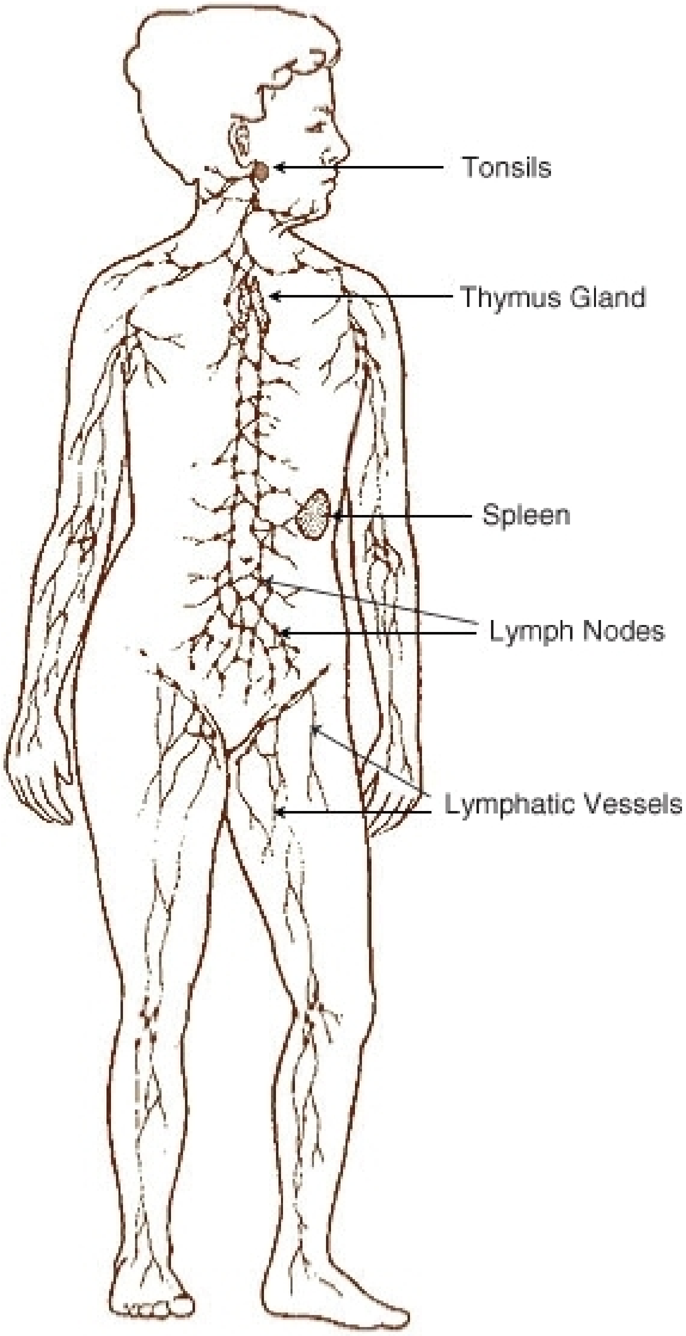

Figure 5.5: Human lymphatic system.

Antigen Receptors

Both B and T cells can "recognize" specific antigens because they have receptor molecules on their surface that bind to particular antigen molecules or pieces of antigen molecules. As shown in **Figure** 5.6, the fit between a receptor molecule and a specific antigen is like a lock and key. Receptors on each B or T cell recognize and bind to just one type of antigen. The human body makes lymphocytes with receptor sites for a huge number of possible antigens that may be encountered throughout a person's life.

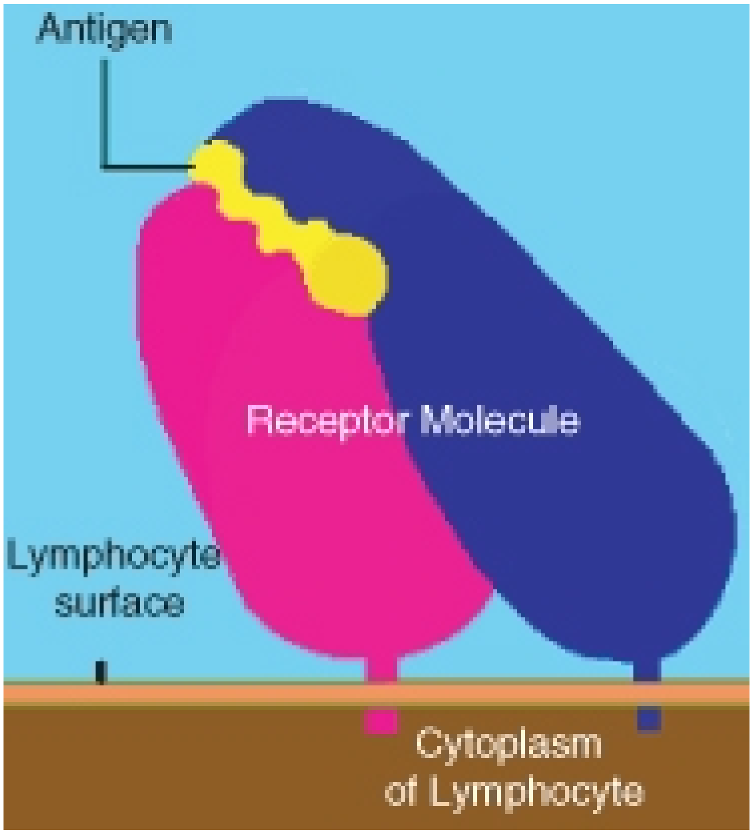

Figure 5.6: A receptor molecule on the surface of a lymphocyte binds to a particular antigen like a lock and key.

Activation of Lymphocytes

Before lymphocytes can function, they must be activated. Activation occurs the first time the cells encounter their specific antigens after leaving the red bone marrow or thymus. Until these circulating B and T cells have been activated, they are called "naïve" cells.

Humoral Immune Response (animation: http://www.cancerresearch.org

B cells are responsible for the humoral immune response. The humoral immune response takes place in blood and lymph and involves the production of antibodies. Antibodies are large, Y-shaped proteins called immunoglobulins (Ig) that recognize and bind to antigens. In humans (and other mammals) there are five types of immunoglobulins: IgA, IgD, IgE, IgG, and IgM. Antibodies are produced by activated B cells.

B Cell Activation

Naïve B cells are activated by an antigen in the sequence of events shown in **Figure** 5.7. A B cell encounters its matching antigen and engulfs it. The B cell then displays fragments of the antigen on its surface. This attracts a helper T cell (which you will read about below). The helper T cell binds to the B cell at the antigen site and releases cytokines. As you read in Lesson 24.1, cytokines are chemical signals used to communicate between cells. Cytokines from the helper T cell stimulate the B cell to develop into plasma cells or memory cells.

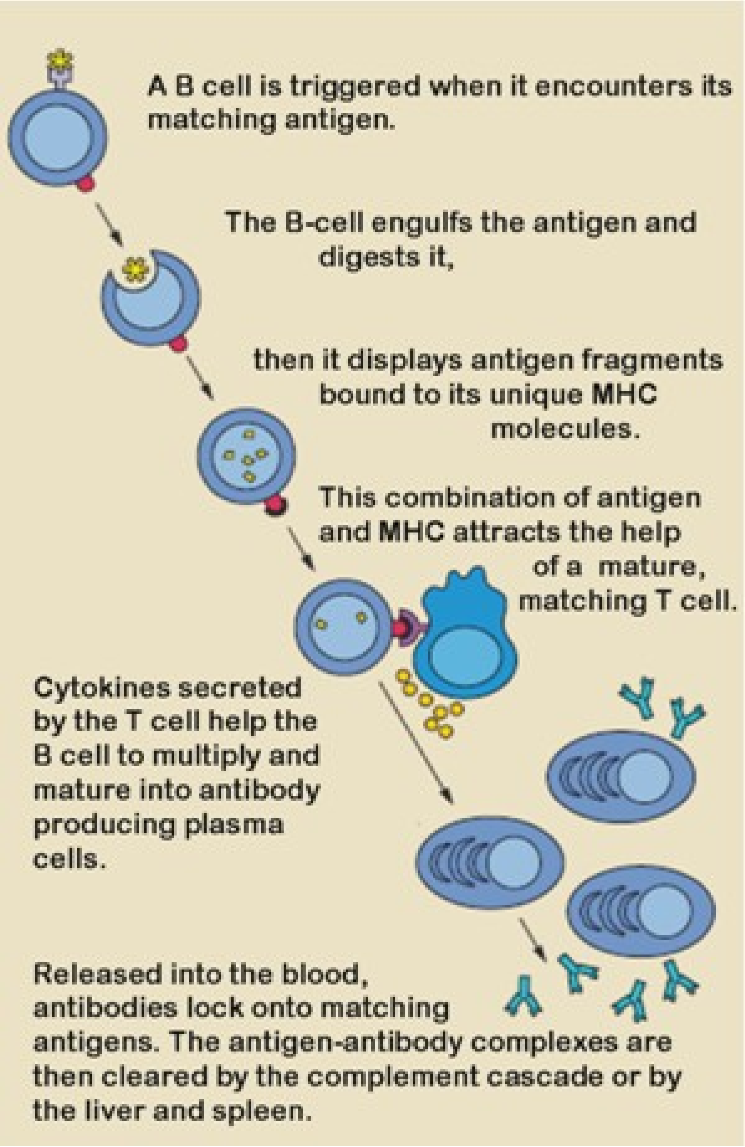
A B cell is triggered when it encounters its matching antigen.
The B-cell engulfs the antigen and digests it,
then it displays antigen fragments bound to its unique MHC molecules.
This combination of antigen and MHC attracts the help of a mature, matching T cell.
Cytokines secreted by the T cell help the B cell to multiply and mature into antibody producing plasma cells.
Released into the blood, antibodies lock onto matching antigens. The antigen-antibody complexes are then cleared by the complement cascade or by the liver and spleen.

Figure 5.7: After engulfing an antigen, a na

Plasma Cells and Antibody Production

Plasma cells are activated B cells that secrete antibodies. They are specialized to act like antibody factories. Antibodies produced by plasma cells circulate in the blood and lymph. Each antibody recognizes and binds to a specific antigen, depending on the plasma cell that produced it and other factors. The binding of an antibody to its matching antigen forms an antigen-antibody complex, as shown in **Figure** 5.8. An antigen-antibody complex flags a pathogen or foreign cell for destruction by phagocytosis. The liver removes antigen-antibody complexes from the blood and the spleen removes them from the lymph.

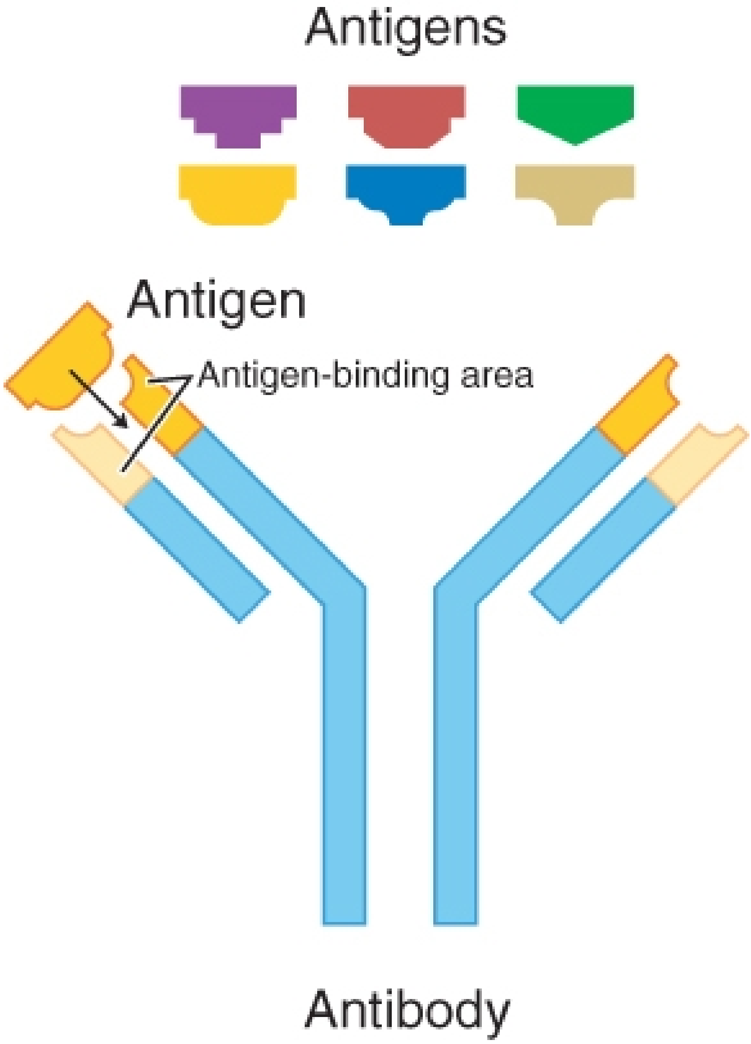

Figure 5.8: An antibody molecule has an area that

Memory Cells

Whereas most plasma cells live just a few days, memory cells live much longer. They may even survive for the lifetime of the individual. Memory cells are activated B (or T) cells that retain a "memory" of a specific pathogen long after an infection is over. They help launch a rapid response against the pathogen if it invades the body in the future. Memory B cells remain in the lymph, ready to produce specific antibodies against the same pathogen if it shows up in body fluids again.

Cell-Mediated Immune Response (Cytotoxic ”killer” T cell animation: http://www.cancerresearch.org/Resources.aspx?id=588)

There are several different types of T cells, including helper, cytotoxic, memory, and regulatory T cells. T cells are responsible for cell-mediated immunity. Cell-mediated immunity involves the destruction of body cells that are infected with pathogens or have become damaged or cancerous.

T Cell Activation

The different types of naïve T cells are activated in the same general way. The mechanism is shown in **Figure** 5.9. It involves B cells or leukocytes such as macrophages. These other cells engulf pathogens in phagocytosis and display parts of the pathogens' antigens on their surface. The cells are then called antigen-presenting cells. When a naïve T cell encounters one of these cells with an antigen matching its own, it begins the activation process. After T cells are activated, the various types of T cells play different roles in the immune response.

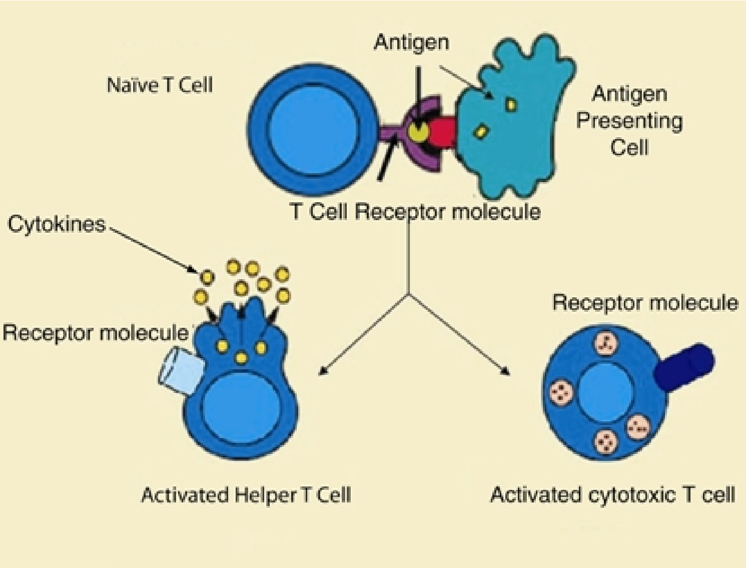

Figure 5.9: A na

Helper T Cells

Activated helper T cells do not kill pathogens or destroy infected cells, but they are still necessary for the immune response. In fact, they are considered to be the ‘‘managers” of the immune response. After activation, helper T cells divide rapidly and secrete cytokines. These chemical signals control the activity of other lymphocytes. As mentioned above, cytokines from helper T cells activate B cells. They also activate other T cells.

Most activated helper T cells die out once a pathogen has been cleared from the body. However, some helper T cells remain in the lymph as memory cells. These memory cells are ready to produce large numbers of antigen-specific helper T cells if they are exposed to the same antigen again in the future.

Cytotoxic T Cells

Helper cells are needed to activate cytotoxic T cells. Activated cytotoxic T cells destroy tumor cells, damaged cells, and cells infected with viruses. They are also involved in the rejection of transplanted organs. Once activated, a cytotoxic T cell divides rapidly and produces an "army" of cells identical to itself. These cells travel throughout the body "searching" for more cells carrying their specific antigen. Whenever they encounter the cells, they destroy them. Illustrated in **Figure** 5.10 is how a cytotoxic T cell destroys a body cell infected with viruses. The cytotoxic T cell releases toxins that form pores, or holes, in the infected cell's membrane. This causes the cell to burst, destroying both the cell and the viruses inside it.

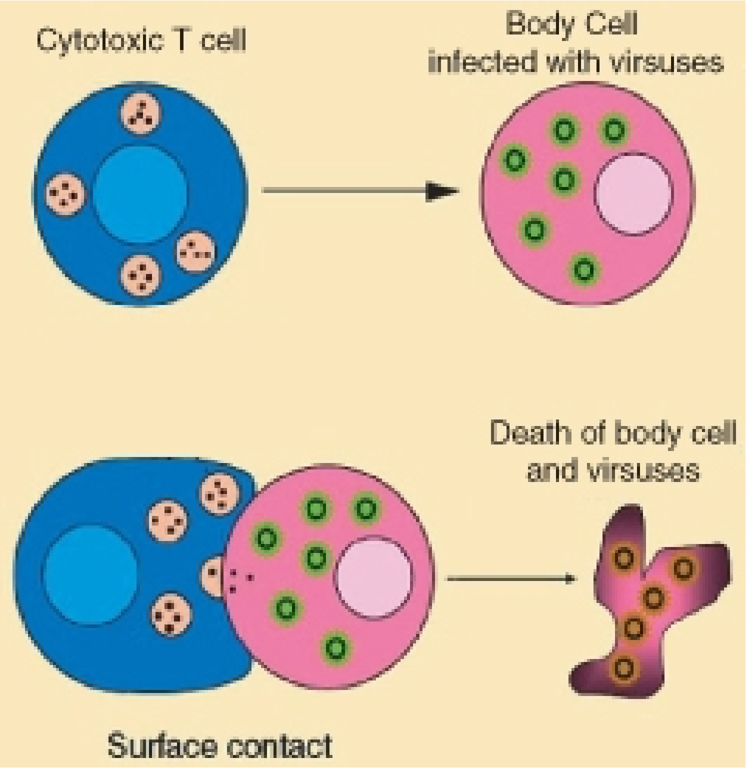
Cytotoxic T cell
Body Cell infected with virsuses
Death of body cell and virsuses
Surface contact

Figure 5.10: A cytotoxic T cell releases toxins that destroy an infected body cell and the viruses it contains.

After cytotoxic T cells bring a viral infection under control, most of the cytotoxic T cells die off. However, some of them remain as memory cells. If the same pathogen tries to infect the body again, the memory cells mount an effective immune response by producing a new army of antigen-specific cytotoxic T cells.

Regulatory T Cells

Regulatory T cells shut down cell-mediated immunity toward the end of an immune response. They also try to suppress any T cells that react against self antigens as though they were foreign. This occurs in automimmune diseases, which you will read about in Lesson 24.3.

Immunity

Memory B and T cells help protect you from re-infection by pathogens that have infected you in the past. Being able to resist a pathogen in this way is called immunity. Immunity can be active or passive.

Active Immunity

Active immunity is immunity that results from a pathogen stimulating an immune response and leaving you with memory cells for the specific pathogen. This happens when a pathogen infects your body and makes you sick. As long as the memory cells survive, the pathogen will be unlikely to re-infect you and make you sick again. In the case of some pathogens, memory cells and active immunity last for the life of the individual.

Active immunity can also occur through immunization. Immunization is deliberate exposure of a person to a pathogen in order to provoke an immune response. The purpose of immunization is to prevent actual infections by the pathogen. The pathogen is typically injected. However, only part of a pathogen, a weakened form of the pathogen, or a dead pathogen is used. This provokes an immune response without making you sick. Diseases you have likely been immunized against include measles, mumps, rubella, whooping cough, and chicken pox.

Passive Immunity

Passive immunity is humoral immunity that results when antibodies to a specific pathogen are transferred to an individual who has never been exposed to the pathogen before. Passive immunity lasts only as long as the antibodies survive in body fluids, generally between a few days and several months.

Passive immunity is acquired by a fetus when it receives antibodies from the mother's blood. It is acquired by an infant when it receives antibodies from the mother's milk. Older children and adults can acquire passive immunity through injection of antibodies into the blood. Injection of antibodies is sometimes used as treatment for a disease, such as measles, when people have not been immunized against the disease.

Active vs. Passive Immunity: http://www.wisc-online.com/objects/ViewObject.aspx?ID=MBY601

Lesson Summary

- The lymphatic system is a major component of the immune system. It filters pathogens from lymph and produces lymphocytes, which are the key cells in an immune response.
- Antigens are proteins that the immune system recognizes as foreign to the body. They trigger the activation of lymphocytes.
- Activated B cells produce antibodies against a pathogen's antigens. Long-lasting memory B cells remain in the body to provide immunity to the specific pathogen.
- Activated T cells destroy tumor cells and cells infected with viruses. Memory T cells remain after an infection to provide antigen-specific immunity.
- Immunity is the ability to resist infection by a pathogen. It can occur by having an immune response to a pathogen or receiving antibodies to a pathogen.

Review Questions

1. List three parts of the lymphatic system and their functions.
2. What are antigens and how do lymphocytes "recognize" them?
3. How do plasma cells form and help fight pathogens?
4. Describe how cytotoxic T cells destroy cells infected with viruses.
5. What type of immune response would occur if bacteria invaded your lymph? Explain your answer.
6. Explain how immunization prevents a disease such as measles.
7. If a disease destroyed a person's helper T cells, how might this affect the immune response?

8. Compare and contrast humoral and cell-mediated immune responses.

Further Reading / Supplemental Links

- Panno, Joseph, Ph.D., Immune System. Facts on File, 2008.
- http://en.wikibooks.org/wiki/Human_Physiology/The_Immune_System
- http://www.acm.uiuc.edu/sigbio/project/lymphatic/index.html
- http://www.cancer.gov/cancertopics/understandingcancer/immunesystem
- http://www.howstuffworks.com/immune-system.htm
- http://www.kidshealth.org/parent/general/body_basics/immune.html
- http://www.kidshealth.org/parent/general/body_basics/spleen_lymphatic.html
- http://www.lymphomation.org/lymphatic.htm
- http://www.niaid.nih.gov/final/immun/immun.htm
- http://www.niaid.nih.gov/publications/immune/the_immune_system.pdf
- http://www.sciencedaily.com/releases/2007/08/070802181939.htm
- http://www.thebody.com/content/art1788.html
- http://en.wikipedia.org

Vocabulary

active immunity Immunity that results from a pathogen stimulating an immune response and leaving you with memory cells for the specific pathogen.

antibody Large, Y-shaped proteins called immunoglobulins (Ig) that recognize and bind to antigens; produced by activated B cells. In humans (and other mammals) there are five types of immunoglobulins: IgA, IgD, IgE, IgG, and IgM.

antigen Any protein that can trigger an immune response because it is foreign to the body; includes proteins on pathogens, cancer cells, and the cells of transplanted organs.

antigen receptor A receptor molecule on the surface of a lymphocyte that binds to a particular antigen like a lock and key.

B lymphocytes (B cells) Lymphocytes that are produced in the red bone marrow and mature in the red bone marrow; can recognize and respond to specific pathogens.

cell-mediated immunity Involves the destruction of body cells that are infected with pathogens or have become damaged or cancerous.

cytotoxic T cells Cells that destroy tumor cells, damaged cells, and cells infected with viruses.

helper T cells Considered to be the ‘‘managers” of the immune response. After activation, helper T cells divide rapidly and secrete cytokines. These chemical signals control the activity of other lymphocytes.

immunity Protection from re-infection by pathogens that have infected you in the past.

immune response The third line of defense; specific to a particular pathogen.

immunization The deliberate exposure of a person to a pathogen in order to provoke an immune response.

lymph Fluid that leaks out of tiny blood vessels, called capillaries, into spaces between cells in tissues.

lymph nodes Small, oval structures located along the lymphatic vessels that act like filters; pathogens filtered out of the lymph at lymph nodes are destroyed by lymphocytes in the nodes.

lymphatic system System that makes lymphocytes; consists of lymphatic organs, lymphatic vessels, lymph, and lymph nodes. Organs of the lymphatic system include the red bone marrow, thymus, spleen, and tonsils.

lymphatic vessels Form a body-wide circulatory system, similar to the arteries and veins of the cardiovascular system; circulate lymph instead of blood.

lymphocytes Type of white blood cells, or leukocytes, primarily involved in the immune response; recognize and help destroy specific foreign invaders in body fluids and cells.

memory cells Memory cells are activated B (or T) cells that retain a "memory" of a specific pathogen long after an infection is over; help launch a rapid response against the pathogen if it invades the body in the future.

passive immunity A humoral immunity that results when antibodies to a specific pathogen are transferred to an individual who has never been exposed to the pathogen before.

phagocytosis The process of engulfing and breaking down pathogens and other unwanted substances.

plasma cells Activated B cells that secrete antibodies.

red bone marrow Found inside many bones, including the hip, breast, and skull bones; produces leukocytes.

regulatory T cells T cells that shut down cell-mediated immunity toward the end of an immune response; also try to suppress any T cells that react against self antigens as though they were foreign.

spleen A gland in the upper abdomen; filters blood and destroys worn-out red blood cells. Lymphocytes in the spleen destroy any pathogens filtered out of the blood.

T lymphocytes (T cells) Lymphocytes that are produced in the red bone marrow and mature in the thymus; can recognize and respond to specific pathogens; includes helper, cytotoxic, memory, and regulatory T cells.

thymus A gland located in the upper chest behind the breast bone; stores and matures lymphocytes.

tonsils Glands on either side of the pharynx in the throat; traps pathogens, which are then destroyed by lymphocytes in the tonsils.

Points to Consider

- Sometimes the immune system makes mistakes and things go wrong. What if the immune system responded to a harmless allergen as though it were a deadly pathogen?
- What if the immune system responded to normal body cells as though they were foreign invaders?
- What if pathogens attacked and destroyed cells of the immune system itself? Would it still be able to function?

5.3 Lesson 24.3: Immune System Diseases

Lesson Objectives

- Explain how allergies occur and list common allergens.
- Describe how autoimmune diseases affect the body.
- Define immunodeficiency and identify ways it can be acquired.
- Explain how HIV is transmitted and how it causes AIDS.

Introduction

The immune system usually protects you from pathogens and keeps you well. However, like any other body system, the immune system can malfunction or become diseased. Sometimes the immune system responds to harmless foreign substances as though they were pathogens. Sometimes it mistakes self for nonself and launches an attack against the body's own cells. Certain diseases can also attack and damage the immune system so it loses the ability to defend the body.

Allergies

An allergy is a disease in which the immune system makes an inflammatory response to a harmless antigen. Any antigen that causes an allergic reaction is called an allergen. You can be exposed to allergens by inhaling or ingesting them or by having direct skin contact with them.

Allergies can vary greatly from person to person. Some people are allergic to many allergens, others to few or none. A tendency to develop allergies can be inherited, so if your mom or dad has allergies, you are more likely to have them as well. Allergy symptoms may be mild or severe. They may develop immediately after exposure to an allergen or not until several days after exposure.

Severity of Allergies

Allergy symptoms are caused by the release of histamines, the chemicals that also stimulate inflammation. The symptoms range from scarcely noticeable to potentially fatal. Typical symptoms of mild allergies include itchy eyes, sneezing, and skin rashes. These symptoms may be uncomfortable, but they are not life threatening. Mild allergy symptoms are often treated with antihistamines. Antihistamines are drugs that reduce or eliminate the effects of histamines.

Immunotherapy, commonly called ‘‘allergy shots,’’ is sometimes recommended for more severe allergies. A person with an allergy is injected with larger and larger amounts of the offending allergen over a period of months or years. This gradually desensitizes the person's immune system to the allergen. Rather than just treating the symptoms of the allergy, immunotherapy reduces the severity of the allergy or eliminates the allergy altogether.

The most severe allergic reaction is anaphylaxis. Anaphylaxis is an allergic response in which there is a sudden, massive release of histamines throughout the body. This causes collapse of the circulatory system and severe constriction of the breathing passages. Without emergency treatment, anaphylaxis is likely to be fatal. Treatment is usually injection of epinephrine. Epinephrine is the "fight-or-flight" hormone that your adrenal glands normally produce when you are in danger. The hormone suppresses non-emergency body processes, including the immune response.

Immediate Hypersensitivity Reaction

When exposure to an antigen causes immediate allergy symptoms, the response is called an immediate hypersensitivity reaction. This is a humoral immune response. Examples of allergens that cause this type of reaction include pollens, bee stings, and peanuts. Anaphylaxis may occur if the allergy is severe.

Allergic rhinitis is a common immediate hypersensitivity reaction. It affects mainly mucous membranes lining the nose. Typical symptoms include runny nose and nasal congestion. Pollens are the most common cause of allergic rhinitis. Tiny pollens of wind-pollinated plants like ragweed (**Figure** 5.11) are the usual culprits. Other causes of allergic rhinitis include mold, animal dander, and dust. Allergic rhinitis may occur seasonally or year-round, depending on its cause.

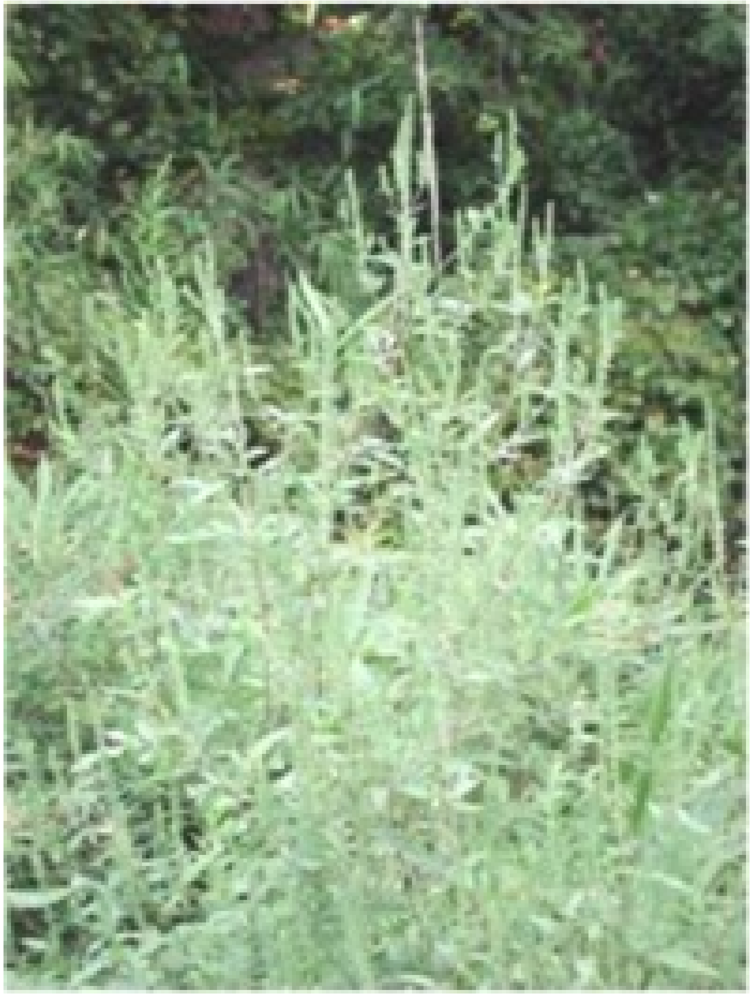

Figure 5.11: Ragweed, a common cause of allergic rhinitis.

Allergic rhinitis is often called hay fever, although pollen—not hay—is the most likely cause. It is called hay fever because it is most common during the time of year when hay is cut. This is also the time of year when plant pollens are most concentrated in outdoor air.

Delayed Hypersensitivity Reaction

When an antigen causes allergy symptoms hours or days after exposure, the response is called a delayed hypersensitivity reaction. This is a cell-mediated immune response. Examples of allergens that cause delayed hypersensitivity reactions include poison ivy, poison oak, and poison sumac. If you have skin contact with these plants and are allergic to them, a rash, like the one in **Figure** 5.12, may develop.

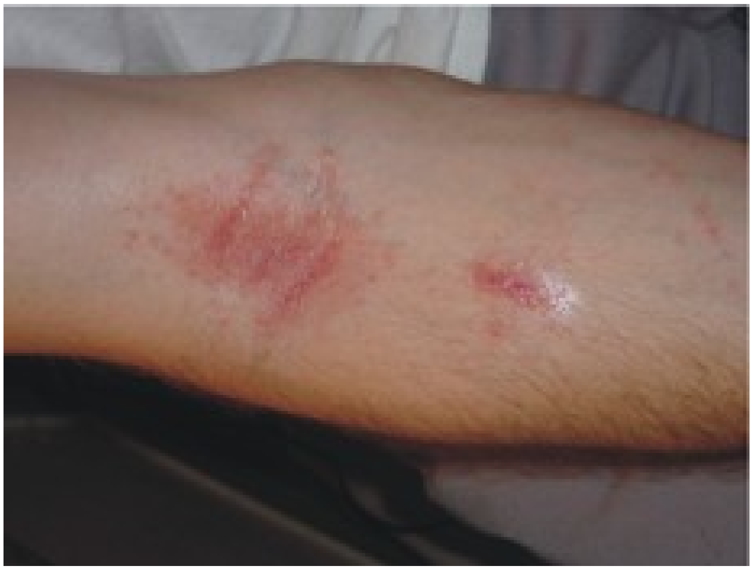

Figure 5.12: Allergic rash caused by contact with poison ivy.

Autoimmune Diseases

Autoimmune diseases occur when the immune system fails to recognize the body's own molecules as self and attacks the body's cells as though they were foreign invaders. Relatively common autoimmune diseases include rheumatoid arthritis, type 1 diabetes mellitus, multiple sclerosis, and systemic lupus erythematosus (**Table** 5.1). These four diseases are described in the table below. They are currently incurable, but treatment can help relieve the symptoms and prevent some of the long-term damage.

Table 5.1: **Common Autoimmune Diseases**

Autoimmune Disease	Object of Immune Attack	Results of Immune Attack	Treatment(s)
Rheumatoid arthritis	Tissues inside joints	Inflammation of joints, causing joint pain and damage and possible loss of mobility	Anti-inflammatory drugs; drugs that suppress the immune system

Table 5.1: (continued)

Autoimmune Disease	Object of Immune Attack	Results of Immune Attack	Treatment(s)
Type 1 diabetes	Insulin-producing cells of the pancreas	Loss of ability to produce insulin, causing too much sugar in the blood and tissue and organ damage	Insulin injections
Multiple sclerosis	Myelin in the brain and spinal cord	Loss of nerve function, causing muscle weakness, fatigue, visual problems, pain, and other symptoms	Corticosteroid drugs; hormones that control the immune system
Systemic lupus erythematosus	Joints, heart, lungs, or other organs	Inflammation of joints or organs, causing serious joint or organ damage and pain	Corticosteroid drugs; drugs that suppress the immune system

The causes of autoimmune diseases are not known for certain. One way autoimmunity may develop is through ‘‘molecular mimicry.” This occurs when a person is infected with pathogens bearing antigens similar to the person’s own molecules. When the immune system mounts an attack against the pathogens, it also attacks body cells with the similar molecules. Some people inherit genes that increase their risk for an autoimmune disease. Female sex hormones may also increase the risk. This may explain why autoimmune diseases are more common in females than males and why they usually begin after puberty.

Immunodeficiency Diseases

Immunodeficiency occurs when one or more components of the immune system are not working normally. As a result, the ability of the immune system to respond to pathogens and other threats is decreased. A person with immunodeficiency may suffer from frequent, life-threatening infections. In other words, an individual with a compromised immune system (for example, a person with AIDS) may be unable to fight off and survive infections by microorganisms that are usually benign. Immunodeficiency can be present at birth or acquired after birth.

Congenital Immunodeficiency

Congenital immunodeficiency is present at birth and usually caused by a genetic disorder. Such disorders are relatively rare. For example, thymic aplasia—a genetic disorder characterized by an absent or abnormal thymus—occurs in about 1 out of 4,000 births. People with thymic aplasia are unable to produce normal T cells. They have frequent infections and increased risk of autoimmune diseases.

Acquired Immunodeficiency

Acquired immunodeficiency occurs when immune function declines in a person who was born with a normal immune system. There are many possible causes for declining immune function. Age is one cause. The immune system naturally becomes less effective as we get older, starting in middle adulthood. This helps explain why older people are more susceptible to disease. Other possible causes of declining immune function include obesity, alcoholism, and illegal drug abuse. In developing countries, malnutrition is a common cause.

Many medications can interfere with normal immune function and cause immunodeficiency. Immune suppressive drugs are deliberately given to people with autoimmune diseases and transplanted organs. Many other drugs have immune suppression as a side effect. Chemotherapy drugs for cancer are especially likely to suppress the immune system.

Several kinds of cancer attack cells of the immune system and cause immunodeficiency. For example, in chronic lymphatic leukemia, abnormal B cells that can't fight infection grow out of control and crowd out healthy B cells. Certain pathogens can also attack cells of the immune system. In fact, the virus known as HIV is the most common cause of immunodeficiency in the world today.

HIV and AIDS

HIV, or human immunodeficiency virus, is the virus that causes AIDS. AIDS stands for acquired immune deficiency syndrome. It is a late stage in the progression of an HIV infection.

HIV Transmission

HIV is transmitted, or spread, through direct contact of mucous membranes or the bloodstream with a body fluid containing HIV. Body fluids that can contain HIV include blood, semen, vaginal fluid, preseminal fluid, and breast milk. Transmission of the virus can occur through sexual contact or use of contaminated hypodermic needles. HIV can also be transmitted through a mother's blood to her baby during late pregnancy or birth or through breast milk after birth. In the past, HIV was transmitted through blood transfusions. Because donated blood is now screened for HIV, the virus is no longer transmitted this way.

HIV and the Immune System

HIV destroys helper T cells. Recall that helper T cells are needed for normal humoral and cell-mediated immunity. When HIV enters a person's bloodstream, proteins on the coat of the virus allow it to fuse with the host's helper T cells. The virus injects its own DNA into the host's helper T cells and uses the T cells' ‘‘machinery” to make copies of itself. The copies of the virus bud off from the host's cells, destroying the cells in the process. Copies of the virus go on to infect other helper T cells throughout the body.

During the first several weeks after HIV infection, the immune system tries to fight off the virus. As shown in **Figure** 5.13, the initial immune response temporarily reduces the number of virus copies in the blood. However, the immune system is unable to destroy the virus, and it continues to multiply in the lymphatic system. How is HIV able to evade the immune system? There are at least two ways:

- The virus undergoes frequent mutations that keep changing the antigens on its coat. This prevents antigen-specific lymphocytes from developing that could destroy the virus.
- The virus uses the host's cell membranes to form is own coat. This covers up viral antigens so they cannot be detected by the host's immune system.

Over the next several years, helper T cells continuously decline in the blood, while copies of the virus keep increasing. As the number of helper T cells declines, so does the ability of the immune system to make an immune response. The HIV-infected person starts showing symptoms of a failing immune system, such as frequent infections.

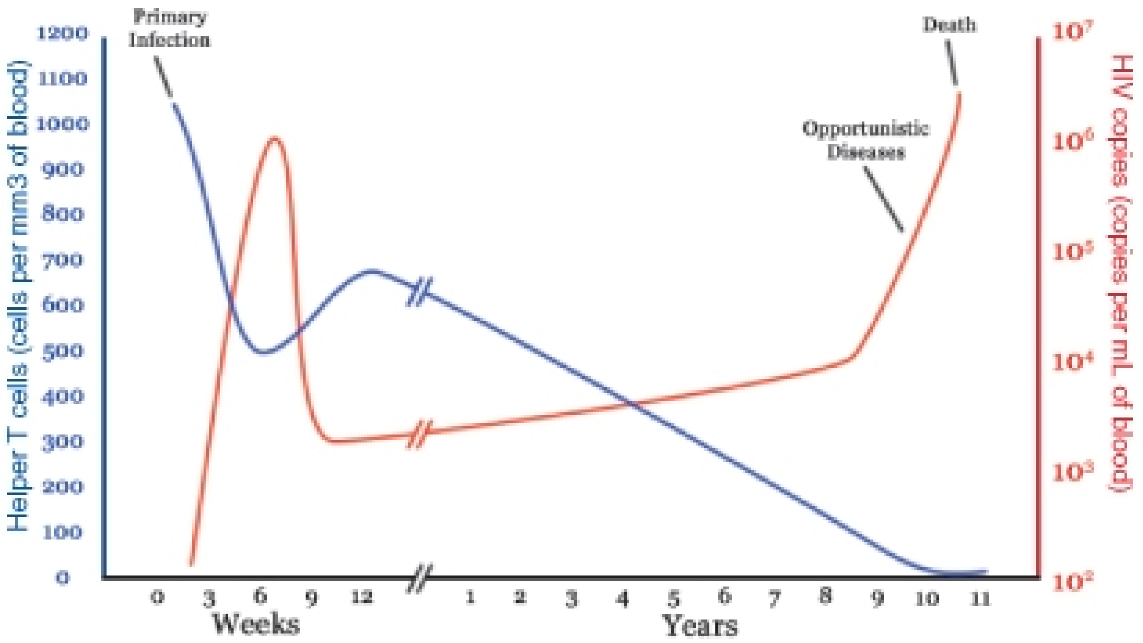

Figure 5.13: Average numbers of helper T cells and HIV copies in untreated HIV infections.

Treatment with antiviral medications can slow down the increase in virus copies, although they do not eliminate the virus altogether. The medications usually lengthen the time between infection with HIV and the development of symptoms. However, currently there is no cure for HIV infection or AIDS and no vaccine to prevent infection, although this is a field of intense study by biomedical scientists.

AIDS

AIDS is not a single disease but a collection of symptoms and diseases. It is the result of years of damage to the immune system by HIV. AIDS is diagnosed when helper T cells fall to a very low level and the infected person develops one or more opportunistic diseases.

Opportunistic diseases are infections and tumors that are rare in people with a healthy immune system but common in immunodeficient people. Opportunistic diseases include pneumocystis pneumonia and Kaposi's sarcoma, a type of cancer. The diseases are called opportunistic because they take advantage of the "opportunity" to infect a person with a damaged immune system that can't fight back. Opportunistic diseases are often the direct cause of death of people with AIDS.

AIDS was first identified in 1981. Since then it has killed more than 25 million people worldwide, many of them children. The hardest hit region is sub-Saharan Africa, where antiviral medications are least available. The worldwide economic toll of AIDS is also enormous.

Lesson Summary

- Allergies occur when the immune system makes an inflammatory response to a harmless antigen, called an allergen.
- Autoimmune diseases occur when the immune system fails to distinguish self from nonself and attacks the body's own cells.

- In an immunodeficiency disease, the immune system does not work normally and cannot defend the body.
- HIV is a virus that attacks cells of the immune system and eventually causes AIDS. It is the chief cause of immunodeficiency in the world today.

Review Questions

1. Describe anaphylaxis.
2. What is an autoimmune disease?
3. List three possible causes of acquired immunodeficiency.
4. Name two ways HIV can be transmitted.
5. Assume that you touch poison sumac and still have not developed a rash 12 hours later. Can you safely assume you are not allergic to the plant? Why or why not?
6. Rheumatic fever is caused by a virus that has antigens similar to molecules in human heart tissues. When the immune system attacks the virus, it also attacks the heart. What type of immune system disease is rheumatic fever? Explain your answer.
7. Draw a timeline to show the progression of an untreated HIV infection. Show how the numbers of HIV copies and helper T cells change through time.
8. Why are opportunistic infections a sign of immunodeficiency?

Further Reading / Supplemental Links

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- http://www.4women.gov/FAQ/autoimmune.htm
- http://en.wikipedia.org

Vocabulary

acquired immunodeficiency Immunodeficiency that occurs when immune function declines in a person who was born with a normal immune system.

AIDS Acquired immune deficiency syndrome; a late stage in the progression of an HIV infection.

allergen Any antigen that causes an allergic reaction.

allergic rhinitis A common immediate hypersensitivity reaction; affects mainly mucous membranes lining the nose; often called hay fever.

allergy A disease in which the immune system makes an inflammatory response to a harmless antigen.

anaphylaxis An allergic response in which there is a sudden, massive release of histamines throughout the body. This causes collapse of the circulatory system and severe constriction of the breathing passages. Without emergency treatment, anaphylaxis is likely to be fatal.

antihistamines Drugs that reduce or eliminate the effects of histamines.

autoimmune diseases Diseases that occur when the immune system fails to recognize the body's own molecules as self and attacks the body's cells as though they were foreign invaders.

delayed hypersensitivity reaction When an antigen causes allergy symptoms hours or days after exposure.

epinephrine The "fight-or-flight" hormone that your adrenal glands normally produce when you are in danger; suppresses non-emergency body processes, including the immune response.

HIV The human immunodeficiency virus, the virus that causes AIDS.

immediate hypersensitivity reaction When exposure to an antigen causes immediate allergy symptoms.

immunodeficiency Occurs when one or more components of the immune system are not working normally; as a result, the ability of the immune system to respond to pathogens and other threats is decreased.

molecular mimicry Occurs when a person is infected with pathogens bearing antigens similar to the person's own molecules; when the immune system mounts an attack against the pathogens, it also attacks body cells with the similar.

opportunistic diseases Infections and tumors that are rare in people with a healthy immune system but common in immunodeficient people; includes pneumocystis pneumonia and Kaposi's sarcoma, a type of cancer.

Points to Consider

You read in this lesson that some types of cancer attack cells of the immune system and cause immunodeficiency. Cancer has previously been described as resulting from a loss of regulation of the cell cycle.

- Why do you think immunodeficiency may lead to some cancers?
- Can you think of a relationship between pathogens, the immune system, and the development of cancer?

5.4 Lesson 24.4: Environmental Problems and Human Health

Lesson Objectives

- Explain how carcinogens cause cancer and list ways that cancer can be treated or prevented.
- Identify causes of air pollution and describe how air pollution affects human health.
- Define bioterrorism and explain how bioterrorism threatens human health.

Introduction

Cancer is one of many human diseases that can be caused by environmental problems. For example, air pollution may increase the risk of lung cancer. It can also cause or worsen asthma, cardiovascular diseases, and other health problems. Bioterrorism is another potential threat to human health. It may lead to severe environmental problems that have the potential to poison large numbers of people or cause epidemics of deadly diseases.

Carcinogens and Cancer

A carcinogen is anything that can cause cancer. Cancer is a disease in which abnormal body cells divide of control. Most carcinogens cause cancer by inducing mutations.

Carcinogens

Carcinogens may be pathogens, chemical substances, or radiation. Carcinogens often occur in nature. For example, some viruses are important carcinogens, causing as many as 15 percent of all human cancers. Different viruses cause different cancers. The human papilloma virus (HPV) is the main cause of cancer of the cervix in females. The hepatitis B virus can cause liver cancer, and the Epstein-Barr virus can cause cancer of the lymph nodes.

Other natural carcinogens include ultraviolet (UV) radiation from the sun. UV radiation is the leading cause of skin cancer. Radon is a natural radioactive gas that seeps into buildings from the ground. Exposure to radon can cause lung cancer. Asbestos can also cause lung cancer. Asbestos is a mineral previously used for insulation and many other purposes. Today, it is largely banned because of its link to cancer.

Humans are exposed to many artificial carcinogens in the environment, including those in tobacco smoke. In fact, tobacco smoke may be the key source of human carcinogen exposure. It contains dozens of carcinogens including nicotine and formaldehyde, which is used to preserve dead bodies. As you will read below, other pollutants in the air can cause cancer as well.

Other artificial carcinogens are or were found in foods. Some food additives, such as certain food dyes, have proven to be carcinogens. Cooking foods at very high temperatures also causes carcinogens to form. For example, a carcinogen called acrylamide forms when carbohydrates are cooked at very high temperatures. It is found in foods such as French fries and potato chips. Barbecued or broiled meats also contain several carcinogens.

How Cancer Occurs

Carcinogens generally cause cancer by inducing mutations in genes that control cell division or other aspects of the cell cycle. The mutations typically occur in two types of genes: tumor-suppressor genes and proto-oncogenes (see chapter titled *Molecular Genetics*). Briefly:

- Tumor-suppressor genes are genes that normally repair damaged DNA or prevent cells with badly damaged DNA from dividing (**Figure A** 5.14). If mutations occur in these genes, they may no longer be able to prevent cells with damaged DNA from dividing (**Figure B** 5.14).
- Proto-oncogenes are genes that normally help regulate cell division. Mutations can turn them into oncogenes. Oncogenes are abnormal genes that stimulate the division of cells with damaged DNA.

Cells that divide uncontrollably form a tumor. A tumor is an abnormal mass of tissue. Tumors may be benign or malignant. Benign tumors remain localized and generally do not harm health. Malignant tumors

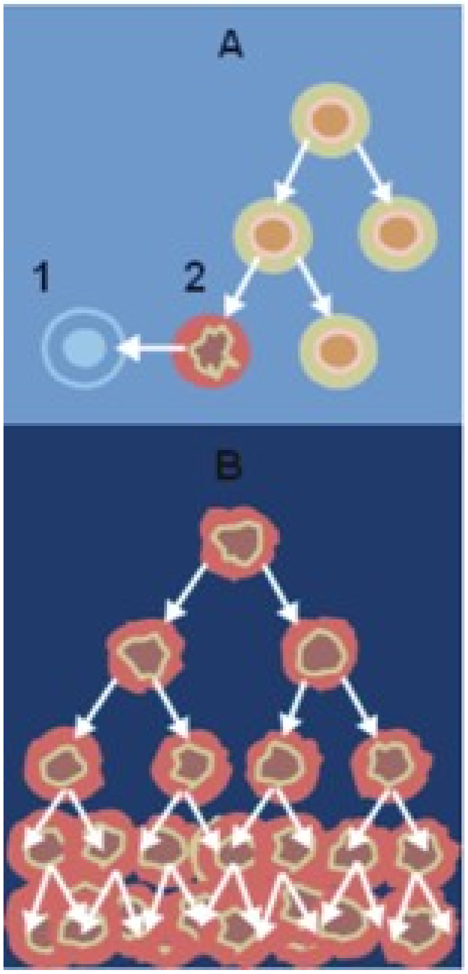

Figure 5.14: A cell with damaged DNA normally is not allowed to divide, so the damage is not passed on to other cells.

are cancer. There are no limits on their growth, so they can invade and damage neighboring tissues. Cells from malignant tumors can also break away from the tumor, enter the circulation, and start growing in another part of the body. This is called metastasis.

Types of Cancer

Cancer is usually classified according to the type of tissue where the cancer begins. Common types of cancer include:

- **Carcinoma**: tumor of epithelial tissues, such as lung tissue.
- **Sarcoma**: tumor of connective tissues, such as bone.
- **Lymphoma**: tumor of lymphatic cells, such as T cells.

Specific cancers are generally named for the organs where the cancers begin. Relatively common cancers include lung, prostate, bladder, and breast cancers. These and several other cancers are listed in the **Table 5.2**. The figure shows which cancers are most common and which cause the most deaths in U.S. adults.

Table 5.2: **Common Cancers among Adult Males and Females in the United States**

Adult Males		Adult Females	
Most Common Cancers (percent of all cancers)	Most Common Causes of Cancer Deaths (percent of all cancer deaths)	Most Common Cancers (percent of all cancers)	Most Common Causes of Cancer Deaths (percent of all cancer deaths)
Prostate cancer(33%)	Lung cancer(31%)	Breast cancer(32%)	Lung cancer(27%)
Lung cancer(13%)	Prostate cancer(10%)	Lung cancer(12%)	Breast cancer(15%)
Colorectal cancer(10%)	Colorectal cancer(10%)	Colorectal cancer(11%)	Colorectal cancer(10%)
Bladder cancer(7%)	Pancreatic cancer(5%)	Endometrial cancer(6%)	Ovarian cancer(6%)

(*Source:* http://en.wikipedia.org/wiki/Cancer, *License:* Creative Commons)

Cancer can also occur in children and teens, but it is rare. Most childhood cancers occur during the first year of life. The most common type of infant cancer is leukemia. It makes up about 30 percent of cancers at this age. With prompt treatment, there is a good chance that an infant with cancer will survive.

Cancer Treatment and Prevention

Most cancers can be treated and some can be cured. The general goal of treatment is to remove the tumor without damaging the rest of the body. Cancer may be treated with a combination of surgery, chemotherapy, and/or radiation. In the past, chemotherapy drugs caused serious side effects. Many of today's chemotherapy drugs target specific molecules in tumors. This reduces damage to normal body cells and causes fewer side effects.

The outcome of cancer treatment depends on factors such as the type of cancer and its stage. The stage of cancer refers to the extent to which the cancer has developed. Generally, early diagnosis and treatment lead to the best chances of survival. That's why it's important for people to be aware of the following warning signs of cancer:

- A change in bowel or bladder habits
- A sore that does not heal
- Unusual bleeding or discharge from any place
- A lump in the breast or other parts of the body
- Chronic indigestion or difficulty in swallowing
- Obvious changes in a wart or mole
- Persistent coughing or hoarseness

Having warning signs of cancer does not mean that you have cancer, but you should see a doctor to be sure. Getting recommended tests for particular cancers, such as colonoscopies for colon cancer, can also help detect cancers early, when chances of a cure are greatest.

Many cancers can be prevented, or at least their risk can be reduced. You can help reduce your risk of cancer by avoiding specific carcinogens and maintaining a healthy lifestyle. Carcinogens you can avoid or limit your exposure to include tobacco smoke, sexually transmitted viruses, improperly cooked foods, and UV radiation. Other lifestyle choices you can make to reduce your risk of cancer include being physically active, eating a low-fat diet, and maintaining a normal weight.

Air Pollution and Illness

An estimated 4.6 million people die each year because of air pollution. Worldwide, air pollution causes more deaths than traffic accidents do. Air pollution harms the respiratory and cardiovascular systems. Both outdoor and indoor air can be polluted and contribute to illness and death.

Outdoor Air Pollution

The concentration of pollutants in outdoor air is indicated by the Air Quality Index. The Air Quality Index (AQI) is a measure of certain pollutants in the air in a given location. The health risks associated with different values of the AQI are shown in the **Table** 5.3 . When the AQI is high, you should limit the time you spend outdoors, especially the time you spend exercising. Avoiding exposure to air pollution can help limit its impact on your health. As you can see from **Table** 5.3, people with certain health problems, including asthma, need to be even more careful about limiting their exposure to air pollution.

Table 5.3: **Air Quality and Health Risk**

Air Quality Index(AQI)	Quality of Air in Terms of Human Health
0–50	Good
51–100	Moderate
101–150	Unhealthy for sensitive groups[1]
151–200	Unhealthy for everyone
201–300	Very unhealthy
301–500	Hazardous

[1] Sensitive groups include people with asthma, heart disease, or other diseases worsened by air pollution.

(*Source:* http://en.wikipedia.org/wiki/Air_Quality_Index, *License:* Creative Commons)

AQI reports to the public generally refer to levels of ground-level ozone and particulates. Ozone is a gas that forms close to the ground when high concentrations of air pollutants are heated by sunlight. Ozone damages both respiratory and cardiovascular systems. For example, it can cause asthma and decrease lung function. It can also convert cholesterol in arteries to plaque, causing cardiovascular disease. In addition, ozone may increase inflammation, which is a symptom of many diseases.

Particulates are tiny particles of solids or liquids suspended in the air. The most concentrated particulate pollution tends to be in the air over densely populated metropolitan areas in developing countries. The primary cause is the burning of fossil fuels by motor vehicles and factories. Particulates settle in airways and lungs and damage the respiratory tract. They can cause asthma and lung cancer. Extremely small particulates may pass through the lungs to the bloodstream and contribute to plaque formation in arteries.

Indoor Air Pollution

Indoor air quality refers to pollutants in the air inside buildings. Indoor air may be more polluted than outdoor air, although with different pollutants. Typical pollutants in indoor air include allergens, mold, bacteria, carbon monoxide, and radon.

Mold and bacteria can be allergens and also cause respiratory system infections. For example, a type of pneumonia, known as Legionnaire's disease, is caused by bacteria that can spread through air conditioning systems. The disease is not common, but it kills many of the people who contract it.

Carbon monoxide is a gas produced by cars, furnaces, and other devices that burn fuel. It replaces oxygen in the blood and quickly leads to death. Initial symptoms of carbon monoxide poisoning include headache, listlessness, and other flu-like symptoms. Loss of consciousness and death can occur within hours. An estimated 40,000 Americans annually seek medical attention for carbon monoxide poisoning. It is also the most common type of fatal poisoning in the U.S. Carbon monoxide is colorless and odorless, but it can be detected with carbon monoxide detectors like the one in **Figure** 5.15.

Sick building syndrome (SBS) is a combination of symptoms associated with working in a particular building, typically an office building. It is most common in new and remodeled buildings. It is usually caused by inadequate ventilation. Chemicals released by new building materials may also contribute to the poor air quality. Generally, conditions improve by increasing ventilation. Symptoms of SBS vary widely. They may include headaches, eye irritation, dry cough, dizziness, and asthma.

Bioterrorism

Bioterrorism is terrorism by intentional release or spread of pathogens. As shown in **Tables** 5.4, 5.5, and 5.6, pathogens used in bioterrorism may include bacteria, viruses, or toxins. Toxins are poisons produced by organisms such as bacteria. The agents may be naturally occurring pathogens or pathogens that have been modified by humans to make them more effective agents of bioterrorism. The agents can spread in a variety of ways, including through air, food, water, direct contact, or cuts in the skin. They have the potential to cause epidemics of deadly human diseases.

Table 5.4: **Classification of Category A Bioterrorism Agents Based Upon Threat to Public Health**

Agent	Type of Pathogen	Mode of Transmission
Anthrax	Bacteria	Air, food, cuts in skin
Smallpox	Virus	Air, direct contact
Botulinum	Toxin	Food, cuts in skin

Figure 5.15: Home carbon monoxide detector

Table 5.5: **Classification of Category B Bioterrorism Agents Based Upon Threat to Public Health**

Agent	Type of Pathogen	Mode of Transmission
Brucellosis	Bacteria	Milk, direct contact
Ricin	Toxin	Air, food, water
Cholera	Bacteria	Food, water

Table 5.6: **Classification of Category C Bioterrorism Agents Based Upon Threat to Public Health**

Agent	Type of Pathogen	Mode of Transmission
Hantavirus	Virus	Air
Tuberculosis	Bacteria	Air

Agents of Bioterrorism

Bioterrorism agents are classified on the basis of their threat to public health, as shown in the tables above. Category A agents (**Table** 5.4) include anthrax and smallpox. Agents in this category pose the greatest threat. They spread easily and cause serious illness or death. Category B agents (**Table** 5.5) are considered less of a threat. They do not spread as easily and are less likely to cause death. Category C agents (**Table** 5.6) are pathogens that are likely to be engineered for bioterrorism in the future. They are easy to produce and have the potential to cause serious illness or death.

Recent Bioterrorism Incidents

Two recent bioterrorism incidents in the U.S. received a great deal of media attention. They heightened public awareness of the threat of bioterrorism. In 2001, letters containing anthrax spores were mailed to several news media offices and two U.S. Senate offices. A total of 22 people were infected, and 5 of them died of anthrax. In 2003, deadly ricin toxin was detected in a letter intended for the White House. The letter was intercepted at a mail-handling facility off White House grounds. Fortunately, the ricin did not cause illness or death.

Lesson Summary

- Carcinogens cause cancer by inducing mutations in genes that normally control cell division or other aspects of the cell cycle.
- Both indoor and outdoor air may contain pollutants that can cause human illness and death.
- In bioterrorism, pathogens are intentionally released or spread and have the potential to cause disease epidemics.

Review Questions

1. What is a carcinogen?
2. How do carcinogens cause cancer?
3. Identify three ways cancer can be treated.

4. List four warning signs of cancer.
5. How can you use the Air Quality Index to protect your health from air pollution?
6. The bacterium that causes plague is classified as a Category A bioterrorism agent. What can you conclude about the bacterium from this classification?
7. Explain why ozone is usually a worse problem in the summer than in the winter in North America.
8. Compare and contrast pollutants in indoor and outdoor air, including their effects on human health.

Further Reading / Supplemental Links

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- http://www.sciencedaily.com/releases/2007/08/070807101114.htm
- http://en.wikipedia.org

Vocabulary

air quality index (AQI) A measure of certain pollutants in the air in a given location.

bioterrorism Terrorism by intentional release or spread of pathogens.

cancer A disease in which abnormal body cells divide of control.

carbon monoxide A gas produced by cars, furnaces, and other devices that burn fuel; replaces oxygen in the blood and quickly leads to death.

carcinogen Anything that can cause cancer; may be pathogens, chemical substances, or radiation.

carcinoma A tumor of epithelial tissues, such as lung tissue.

lymphoma A tumor of lymphatic cells, such as T cells.

oncogenes Abnormal genes that stimulate the division of cells with damaged DNA.

ozone A gas that forms close to the ground when high concentrations of air pollutants are heated by sunlight.

particulates Tiny particles of solids or liquids suspended in the air; primarily formed by the burning of fossil fuels by motor vehicles and factories.

proto-oncogenes Genes that normally help regulate cell division.

sarcoma A tumor of connective tissues, such as bone.

sick building syndrome (SBS) A combination of symptoms associated with working in a particular building, typically an office building.

tumor An abnormal mass of tissue.

tumor-suppressor genes Genes that normally repair damaged DNA or prevent cells with badly damaged DNA from dividing.

Points to Consider

High levels of certain hormones can increase the risk of some types of cancer. For example, high levels of estrogen can increase the risk of breast cancer. Estrogen is a female sex hormone.

- What are sex hormones?
- How do sex hormones normally affect the body?
- How are male and female sex hormones different?

Chapter 6

Viruses

6.1 Viruses

Lesson Objectives

- Describe the structure of viruses.
- Outline the discovery and origins of viruses.
- Explain how viruses replicate.
- Explain how viruses cause human disease.
- Describe how viruses can be controlled.
- Identify how viruses are used in research and medicine.

Lesson Vocabulary

- capsid
- latency
- vaccine
- virion

Introduction

At the end of the last lesson, you were asked which of the three domains of life do viruses belong to. Did you figure it out? None. Why? Viruses are usually considered to be nonliving. Viruses do not meet most of the criteria of life. They are not even cells.

An overview of viruses can be seen at http://www.youtube.com/user/khanacademy#p/c/7A9646BC5110CF64/17/0h5

Characteristics of Viruses

An individual virus is called a **virion.** It is a tiny particle much smaller than a prokaryotic cell. Because viruses do not consist of cells, they also lack cell membranes, cytoplasm, ribosomes, and other cell organelles. Without these structures, they are unable to make proteins or even reproduce on their own. Instead, they must depend on a host cell to synthesize their proteins and to make copies of themselves. Viruses infect

Figure 6.1: Viruses (Watch Youtube Video)
http://www.ck12.org/flexbook/embed/view/107

and live inside the cells of living organisms. When viruses infect the cells of their host, they may cause disease. For example, viruses cause AIDS, influenza (flu), chicken pox, and the common cold.

Although viruses are not classified as living things, they share two important traits with living things. They have genetic material, and they can evolve. This is why the classification of viruses has been controversial. It calls into question just what it means to be alive. What do you think? How would you classify viruses?

Structure and Classification of Viruses

Viruses vary in their structure. The structure of a virus determines how it is classified.

Structure of Viruses

A virus particle consists of DNA or RNA within a protective protein coat called a **capsid.** The shape of the capsid may vary from one type of virus to another, as shown in **Figure** 6.2.

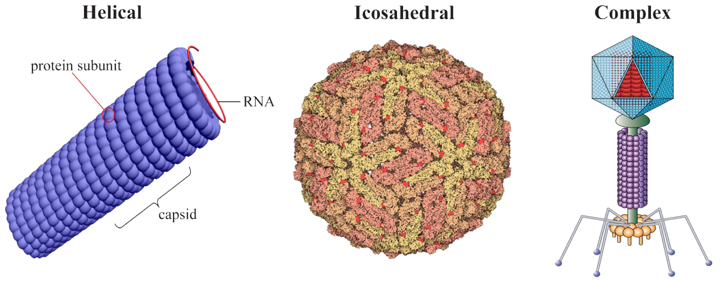


Figure 6.2: Capsid Shapes in Viruses. Three shapes of viral capsids are shown here. They are helical (spiral), icosahedral (20-sided), and complex. Viruses with complex shapes may have extra structures such as protein tails.

Some viruses have an envelope of phospholipids and proteins. The envelope is made from portions of the host's cell membrane. It surrounds the capsid and helps protect the virus from the host's immune system. The envelope may also have receptor molecules that can bind with host cells. They make it easier for the virus to infect the cells.

Classification of Viruses

Viruses are classified on the basis of several traits. For example, they may be classified by capsid shape, presence or absence of an envelope, and type of nucleic acid. **Table** 6.1 gives four examples of virus families and their traits.

Table 6.1: **Virus Classification: Four Examples**

Virus Family	Capsid Shape	Envelope Present?	Type of Nucleic Acid	Disease Caused by a Virus in this Family
Adenovirus	icosahedral	no	DNA	acute respiratory disease
Herpesviruses	icosahedral	yes	DNA	chicken pox
Orthomyxoviruses	helical	yes	RNA	influenza
Coronaviruses	complex	yes	RNA	common cold

Table 13.6 Most systems of classifying viruses identify at least 20 virus families. Only 4 are shown here. Have any of these viruses made you sick?

Discovery and Origin of Viruses

Viruses are so small that they can be seen only with an electron microscope. Before electron microscopes were invented, scientists knew viruses must exist. How did they know? They had demonstrated that particles smaller than bacteria cause disease.

Discovery of Viruses

Researchers used special filters to remove bacteria from tissues that were infected. If bacteria were causing the infection, the filtered tissues should no longer be able to make other organisms sick. However, the filtered tissues remained infective. This meant that something even smaller than bacteria was causing the infection.

Scientists did not actually see viruses for the first time until the 1930s. That's when the electron microscope was invented. The virus shown in **Figure** 6.3 was the first one to be seen.

Origin of Viruses

Where did viruses come from? How did the first viruses arise? The answers to these questions are not known for certain. Several hypotheses have been proposed. The two main hypothesis are stated below. Both may be valid and explain the origin of different viruses.

- Small viruses started as runaway pieces of nucleic acid that originally came from living cells such as bacteria.
- Large viruses were once parasitic cells inside bigger host cells. Over time, genes needed to survive and reproduce outside host cells were lost.

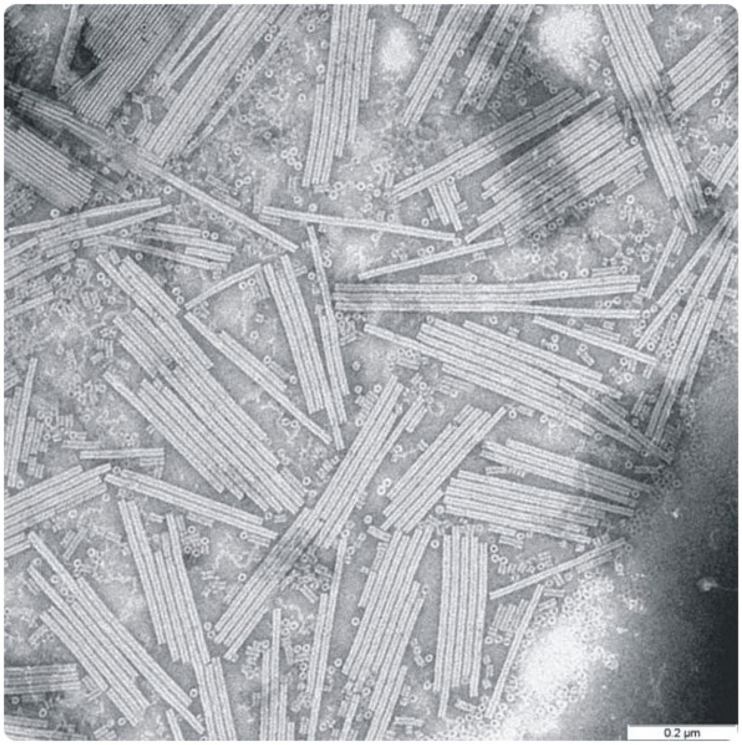


Figure 6.3: Tobacco Mosaic Virus. This tobacco mosaic virus was the first virus to be discovered. It was first seen with an electron microscope in 1935.

Replication of Viruses

Populations of viruses do not grow through cell division because they are not cells. Instead, they use the machinery and metabolism of a host cell to produce new copies of themselves. After infecting a host cell, a virion uses the cell's ribosomes, enzymes, ATP and other components to replicate. Viruses vary in how they do this. For example:

- Some RNA viruses are translated directly into viral proteins in ribosomes of the host cell. The host ribosomes treat the viral RNA as though it were the host's own mRNA.
- Some DNA viruses are first transcribed in the host cell into viral mRNA. Then the viral mRNA is translated by host cell ribosomes into viral proteins.

In either case, the newly made viral proteins assemble to form new virions. The virions may then direct the production of an enzyme that breaks down the host cell wall. This allows the virions to burst out of the cell. The host cell is destroyed in the process. The newly released virus particles are free to infect other cells of the host.

Viruses and Human Disease

Viruses cause many human diseases. In addition to the diseases mentioned above, viruses cause rabies, measles, diarrheal diseases, hepatitis, polio, and cold sores (see **Figure** 6.4). Viral diseases range from mild to fatal. One way viruses cause disease is by causing host cells to burst open and die. Viruses may also cause disease without killing host cells. They may cause illness by disrupting homeostasis in host cells.

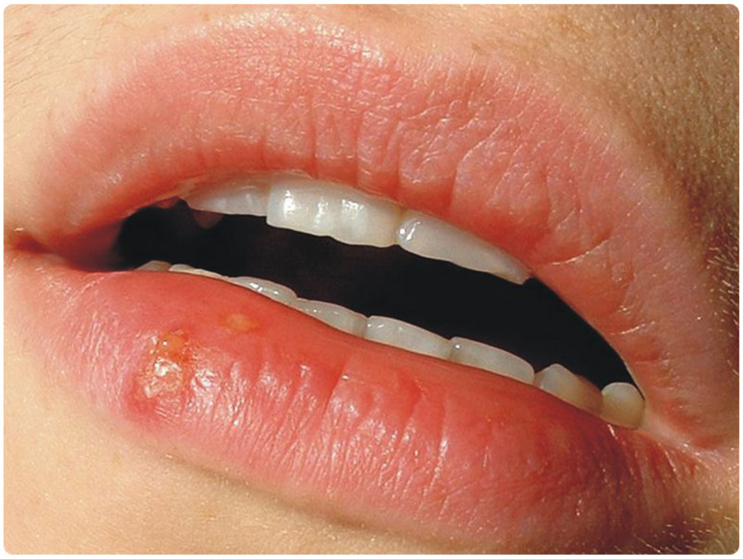


Figure 6.4: Cold Sore. Cold sores are caused by a herpes virus.

Some viruses live in a dormant state inside the body. This is called **latency**. For example, the virus that causes chicken pox may infect a young child and cause the short-term disease chicken pox. Then the virus may remain latent in nerve cells within the body for decades. The virus may re-emerge later in life as the disease called shingles. In shingles, the virus causes painful skin rashes with blisters (see **Figure** 6.5).

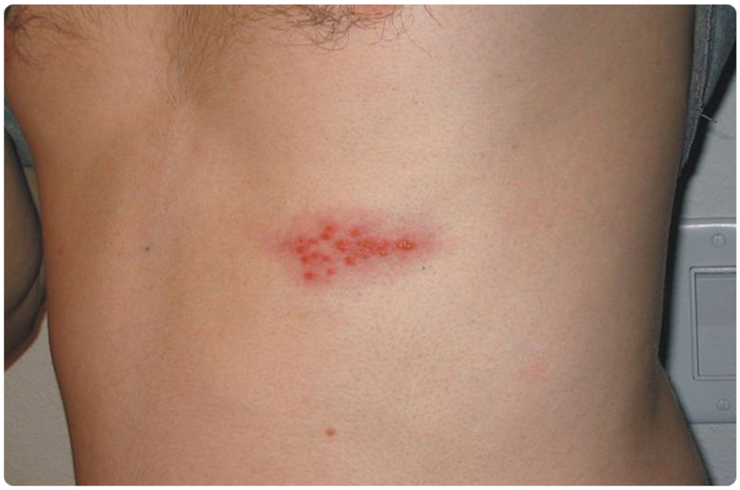


Figure 6.5: Shingles. Shingles is a disease caused by the same virus that causes chicken pox.

Some viruses can cause cancer. For example, human papillomavirus (HPV) causes cancer of the cervix in females. Hepatitis B virus causes cancer of the liver. A viral cancer is likely to develop only after a person has been infected with a virus for many years.

Control of Viruses

Viral diseases can be difficult to treat. They live inside the cells of their host, so it is hard to destroy them without killing host cells. Antibiotics also have no effect on viruses. Antiviral drugs are available, but only for a limited number of viruses.

Many viral diseases can be prevented by giving people vaccines (see **Figure** 6.6). A **vaccine** is a substance that contains pathogens such as viruses. The pathogens have been changed in some way so they no longer cause disease. However, they can still provoke a response from the host's immune system. This results in immunity, or the ability to resist the pathogen. Vaccines have been produced for the viruses that cause measles, chicken pox, mumps, polio, and several other diseases.

Figure 6.6: Vaccination. A child receives a vaccine to prevent a viral disease. How does the vaccine prevent the disease?

Viruses in Research and Medicine

Viruses are important tools in scientific research and medicine. Viral research has increased our understanding of fundamental biological processes involving DNA, RNA, and proteins. Viruses that infect cancer cells are being studied for their use in cancer treatment. Viruses are also being used in gene therapy to treat genetic disorders, as explained in **Figure** 6.7.

Lesson Summary

- Viruses are tiny particles, smaller than prokaryotic cells. They are not cells and cannot replicate without help, but they have nucleic acids and can evolve.
- Viruses can be classified on the basis of capsid shape, presence or absence of an envelope, and type of nucleic acid.
- Viruses were assumed to exist before they were first seen with an electron microscope in the 1930s. Multiple hypotheses for viral origins have been proposed.
- After infecting a host cell, a virus uses the cell's machinery and metabolism to produce new copies of itself.
- Viruses cause many human diseases by killing host cells or disturbing their homeostasis. Viruses are not affected by antibiotics. Several viral disease can be treated with antiviral drugs or prevented with vaccines.
- Viruses are useful tools in scientific research and medicine. Viruses help us understand molecular biology. They are also used in gene therapy.

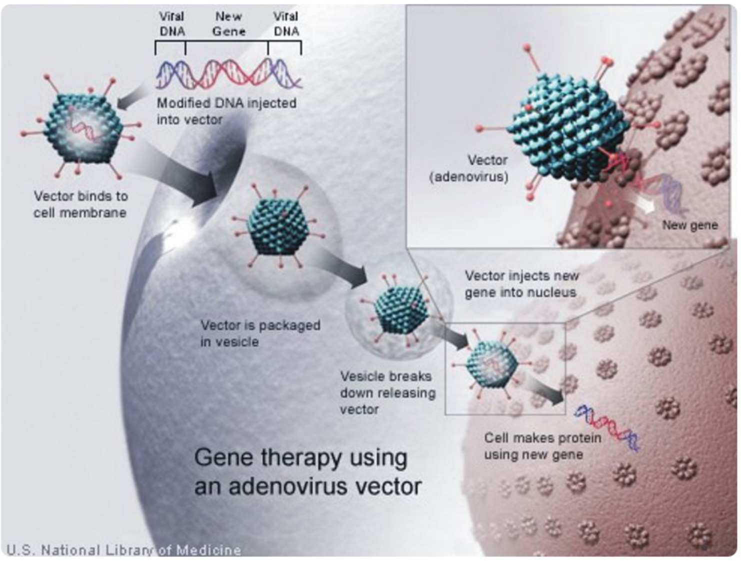

Viral DNA
New Gene
Viral DNA
Modified DNA injected into vector
Vector binds to cell membrane
Vector (adenovirus)
New gene
Vector injects new gene into nucleus
Vector is packaged in vesicle
Vesicle breaks down releasing vector
Cell makes protein using new gene
Gene therapy using an adenovirus vector
U.S. National Library of Medicine

Figure 6.7: Using a Virus in Gene Therapy. A normal human gene is inserted into a virus. The virus carries the gene into a human host cell. The gene enters the nucleus and becomes part of the DNA. The normal gene can then be used to make normal proteins. It can also be copied and passed to daughter cells in the host.

Lesson Review Questions

Recall

1. How do viruses differ from living things? How are they similar to living things?
2. Describe variation in capsid shape in viruses.
3. State two hypotheses for the origin of viruses.
4. Describe how viruses replicate.
5. How do viruses cause human disease?

Apply Concepts

6. Apply lesson concepts to decide how strep throat and flu can be treated or prevented. Create a chart to summarize your ideas.

7. Viruses often infect bacteria. Some of them destroy the bacterial cells they infect. How could this information be applied to finding a cure for bacterial infections?

Think Critically

8. Why did scientists think viruses must exist even before they ever saw them with an electron microscope?

9. Why are viruses especially useful tools for understanding molecular biology? What might scientists learn by studying how viruses invade and use host cells?

Chapter 7

Meiosis and Mendelian Genetics

7.1 Reproduction and Meiosis

Lesson Objectives

- Compare and contrast asexual and sexual reproduction.
- Give an overview of sexual reproduction, and outline the phases of meiosis.
- Explain why sexual reproduction leads to variation in offspring.
- Define life cycle, and identify different types of sexual life cycles.

Vocabulary

asexual reproduction crossing-over diploid cell
egg fertilization gamete
gametogenesis haploid cell independent assortment
life cycle meiosis sexual reproduction
sperm zygote

Introduction

Cell division is how organisms grow and repair themselves. It is also how they produce offspring. Many single-celled organisms reproduce by binary fission. The parent cell simply divides to form two daughter cells that are identical to the parent. In many other organisms, two parents are involved, and the offspring are not identical to the parents. In fact, each offspring is unique. Look at the family in **Figure** 7.1. The children resemble their parents, but they are not identical to them. Instead, each has a unique combination of characteristics inherited from both parents. In this lesson, you will learn how this happens.

Figure 7.1: Family Portrait: Mother, Daughter, Father, and Son. Children resemble their parents, but they are never identical to them. Do you know why this is the case?

Reproduction: Asexual vs. Sexual

Reproduction is the process by which organisms give rise to offspring. It is one of the defining characteristics of living things. There are two basic types of reproduction: asexual reproduction and sexual reproduction.

Asexual Reproduction

Asexual reproduction involves a single parent. It results in offspring that are genetically identical to each other and to the parent. All prokaryotes and some eukaryotes reproduce this way. There are several different methods of asexual reproduction. They include binary fission, fragmentation, and budding.

- Binary fission occurs when a parent cell splits into two identical daughter cells of the same size. This process was described in detail in Lesson 5.1.
- Fragmentation occurs when a parent organism breaks into fragments, or pieces, and each fragment develops into a new organism. Starfish, like the one in **Figure** 7.2, reproduce this way. A new starfish can develop from a single ray, or arm.
- Budding occurs when a parent cell forms a bubble-like bud. The bud stays attached to the parent cell while it grows and develops. When the bud is fully developed, it breaks away from the parent cell and forms a new organism. Budding in yeast is shown in **Figure** 7.3.

Figure 7.2: Starfish reproduce by fragmentation.

Asexual reproduction can be very rapid. This is an advantage for many organisms. It allows them to crowd out other organisms that reproduce more slowly. Bacteria, for example, may divide several times

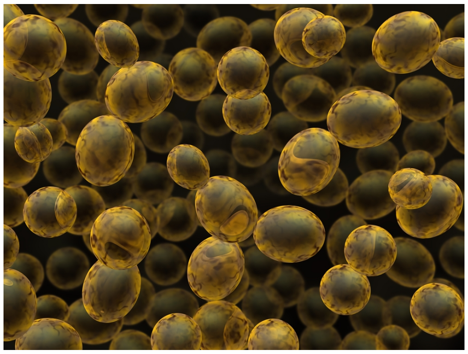


Figure 7.3: Yeast reproduces by budding. Both are types of asexual reproduction.

per hour. Under ideal conditions, 100 bacteria can divide to produce millions of bacterial cells in just a few hours! However, most bacteria do not live under ideal conditions. If they did, the entire surface of the planet would soon be covered with them. Instead, their reproduction is kept in check by limited resources, predators, and their own wastes. This is true of most other organisms as well.

Sexual Reproduction

Sexual reproduction involves two parents. As you can see from **Figure** 7.5, in sexual reproduction, parents produce reproductive cells—called **gametes**—that unite to form an offspring. Gametes are **haploid** cells. This means they contain only half the number of chromosomes found in other cells of the organism. Gametes are produced by a type of cell division called meiosis, which is described in detail below. The process in which two gametes unite is called **fertilization**. The fertilized cell that results is referred to as a **zygote**. A zygote is **diploid** cell, which means that it has twice the number of chromosomes as a gamete.

Mitosis, Meiosis and Sexual Reproduction is discussed at http://www.youtube.com/user/khanacademy#p/c/7A9646B

Figure 7.4: Mitosis, meiosis and sexual reproduction. Understanding gametes, zygotes, and haploid / diploid numbers. (Watch Youtube Video) http://www.youtube.com/v/kaSIjIzAtYA?f=videosamp;c=ytapi-CK12Foundation-Flexrwikiimport-fg5akohk-0amp;d=AT8BNcsNZiISDLhsoSt-gqIO88HsQjpE1a8d1GxQnGDmamp;app=youtube_gdata

Meiosis and Gametogenesis

The process that produces haploid gametes is meiosis (see **Figure** 7.5). **Meiosis** is a type of cell division in which the number of chromosomes is reduced by half. It occurs only in certain special cells of the organisms. During meiosis, homologous chromosomes separate, and haploid cells form that have only one chromosome from each pair. Two cell divisions occur during meiosis, and a total of four haploid cells

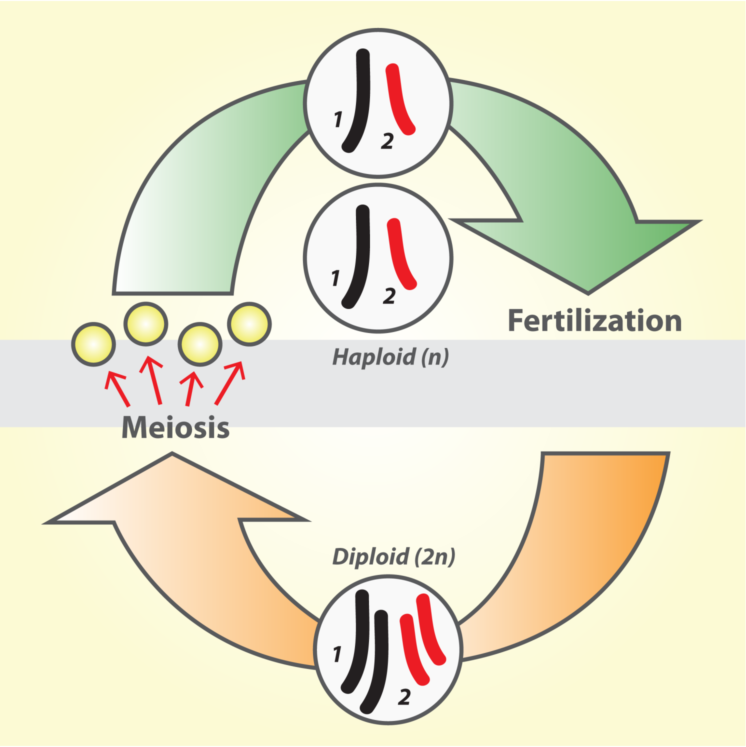


Figure 7.5: Cycle of Sexual Reproduction. Sexual reproduction involves the production of haploid gametes by meiosis. This is followed by fertilization and the formation of a diploid zygote. The number of chromosomes in a gamete is represented by the letter n. Why does the zygote have 2n, or twice as many, chromosomes?

are produced. The two cell divisions are called meiosis I and meiosis II. The overall process of meiosis is summarized in **Figure** 7.6. It is also described in detail below. You can watch an animation of meiosis at this link: http://www.youtube.com/watch?v=D1_-mQS_FZ0&#38;#38;feature=related.

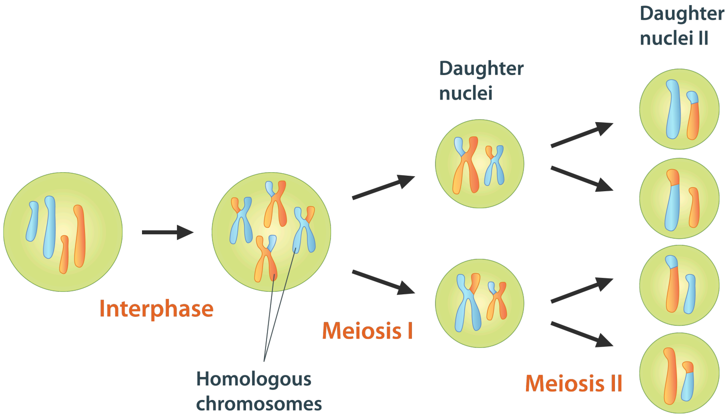


Figure 7.6: Overview of Meiosis. During meiosis, homologous chromosomes separate and go to different daughter cells. This diagram shows just the nuclei of the cells.

Phases of Meiosis

Meiosis I begins after DNA replicates during interphase. In both meiosis I and meiosis II, cells go through the same four phases as mitosis. However, there are important differences between meiosis I and mitosis. The flowchart in **Figure** 7.7 shows what happens in both meiosis I and II. You can follow the changes in the flowchart as you read about them below.

Meiosis I

1. Prophase I: The nuclear envelope begins to break down, and the chromosomes condense. Centrioles start moving to opposite poles of the cell, and a starts begins to grow. Importantly, homologous chromosomes pair up, which is unique to prophase I. In prophase of mitosis and meiosis II, homologous chromosomes do not form pairs in this way.
2. Metaphase I: Spindle fibers attach to the paired homologous chromosomes. The paired chromosomes line up along the equator of the cell. This occurs only in metaphase I. In metaphase of mitosis and meiosis II, it is sister chromatids that line up along the equator of the cell.
3. Anaphase I: Spindle fibers shorten, and the chromosomes of each homologous pair start to separate from each other. One chromosome of each pair moves toward one pole of the cell, and the other chromosome moves toward the opposite pole.
4. Telophase I and Cytokinesis: The spindle breaks down, and new nuclear membranes form. The cytoplasm of the cell divides, and two haploid daughter cells result. The daughter cells each have a random assortment of chromosomes, with one from each homologous pair. Both daughter cells go on to meiosis II.

Meiosis II

1. Prophase II: The nuclear envelope breaks down and the spindle begins to form in each haploid daughter cell from meiosis I. The centrioles also start to separate.

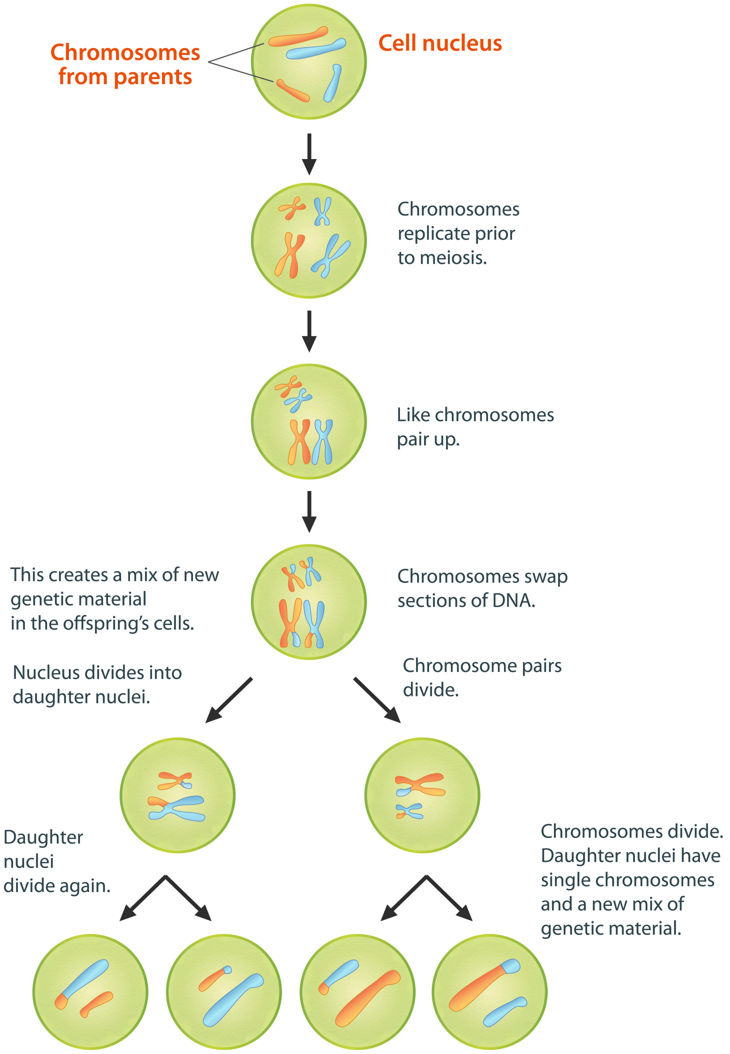

Chromosomes from parents
Cell nucleus
Chromosomes replicate prior to meiosis.
Like chromosomes pair up.
This creates a mix of new genetic material in the offspring's cells.
Chromosomes swap sections of DNA.
Nucleus divides into daughter nuclei.
Chromosome pairs divide.
Daughter nuclei divide again.
Chromosomes divide. Daughter nuclei have single chromosomes and a new mix of genetic material.

Figure 7.7: Phases of Meiosis. This flowchart of meiosis shows meiosis I in greater detail than meiosis II. Meiosis I

2. Metaphase II: Spindle fibers line up the sister chromatids of each chromosome along the equator of the cell.
3. Anaphase II: Sister chromatids separate and move to opposite poles.
4. Telophase II and Cytokinesis: The spindle breaks down, and new nuclear membranes form. The cytoplasm of each cell divides, and four haploid cells result. Each cell has a unique combination of chromosomes.

Gametogenesis

At the end of meiosis, four haploid cells have been produced, but the cells are not yet gametes. The cells need to develop before they become mature gametes capable of fertilization. The development of haploid cells into gametes is called **gametogenesis**. Gametogenesis may differ between males and females. Male gametes are called **sperm**. Female gametes are called **eggs**. In human males, for example, the process that produces mature sperm cells is called spermatogenesis. During this process, sperm cells grow a tail and gain the ability to "swim," like the human sperm cell shown in **Figure** 7.8. In human females, the process that produces mature eggs is called oogenesis. Just one egg is produced from the four haploid cells that result from meiosis. The single egg is a very large cell, as you can see from the human egg in **Figure** 7.8.

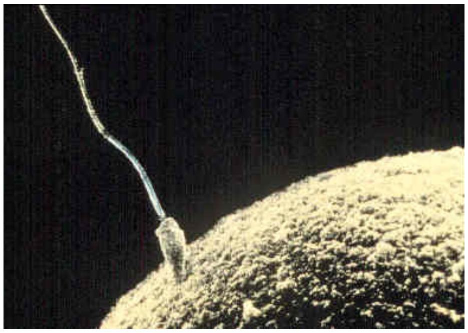


Figure 7.8: A human sperm is a tiny cell with a tail. A human egg is much larger. Both cells are mature haploid gametes that are capable of fertilization. What process is shown in this photograph?

Sexual Reproduction and Genetic Variation

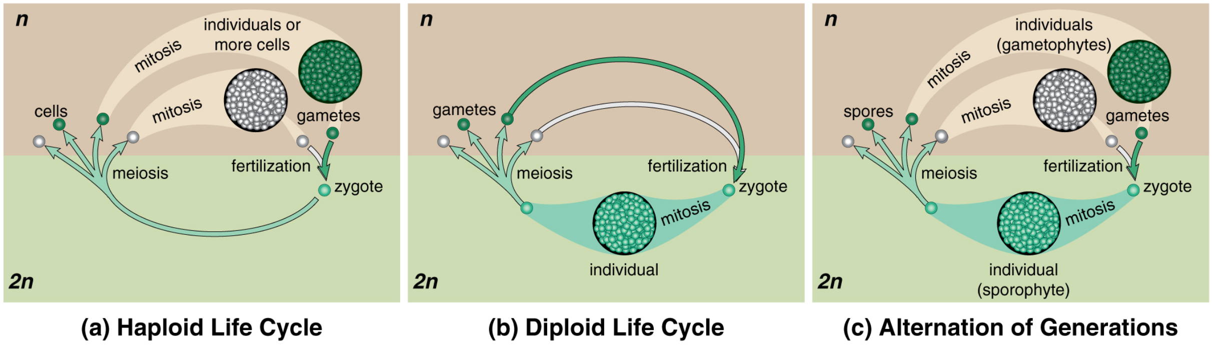
Sexual reproduction results in offspring that are genetically unique. They differ from both parents and also from each other. This occurs for a number of reasons.

- When homologous chromosomes pair up during meiosis I, crossing-over can occur. **Crossing-over** is the exchange of genetic material between homologous chromosomes. It results in new combinations of genes on each chromosome.
- When cells divide during meiosis, homologous chromosomes are randomly distributed to daughter cells, and different chromosomes segregate independently of each other. This called is called **independent assortment**. It results in gametes that have unique combinations of chromosomes.
- In sexual reproduction, two gametes unite to produce an offspring. But which two of the millions of possible gametes will it be? This is likely to be a matter of chance. It is obviously another source of genetic variation in offspring.

All of these mechanisms working together result in an amazing amount of potential variation. Each human couple, for example, has the potential to produce more than 64 trillion genetically unique children. No wonder we are all different!

Sexual Reproduction and Life Cycles

Sexual reproduction occurs in a cycle. Diploid parents produce haploid gametes that unite and develop into diploid adults, which repeat the cycle. This series of life stages and events that a sexually reproducing organism goes through is called its life cycle. Sexually reproducing organisms can have different types of life cycles. Three are represented in **Figure** 7.9 and described following sections.



(a) Haploid Life Cycle **(b) Diploid Life Cycle** **(c) Alternation of Generations**

Figure 7.9: Life cycles can vary in sexually reproducing organisms. Three types of sexual life cycles are shown here. Do you see how they differ? The letter

Haploid Life Cycle

The haploid life cycle is the simplest life cycle. It is found in many single-celled organisms. Organisms with a haploid life cycle spend the majority of their lives as haploid gametes. When the haploid gametes fuse, they form a diploid zygote. It quickly undergoes meiosis to produce more haploid gametes that repeat the life cycle.

Diploid Life Cycle

Organisms with a diploid life cycle spend the majority of their lives as diploid adults. When they are ready to reproduce, they undergo meiosis and produce haploid gametes. Gametes then unite in fertilization and form a diploid zygote. The zygote develops into a diploid adult that repeats the life cycle. Can you think of an organism with a diploid life cycle? (*Hint:* What type of life cycle do humans have?)

Alternation of Generations

Organisms that have a life cycle with alternating generations switch back and forth between diploid and haploid stages. Organisms with this type of life cycle include plants, algae, and some protists. These life cycles may be quite complicated. You can read about them in later chapters.

Lesson Summary

- Asexual reproduction involves one parent and produces offspring that are genetically identical to each other and to the parent. Sexual reproduction involves two parents and produces offspring that

are genetically unique.
- During sexual reproduction, two haploid gametes join in the process of fertilization to produce a diploid zygote. Meiosis is the type of cell division that produces gametes. It involves two cell divisions and produces four haploid cells.
- Sexual reproduction has the potential to produce tremendous genetic variation in offspring. This variation is due to independent assortment and crossing-over during meiosis and random union of gametes during fertilization.
- A life cycle is the sequence of stages an organisms goes through from one generation to the next. Organisms that reproduce sexually can have different types of life cycles, such as haploid or diploid life cycles.

Lesson Review Questions

Recall

1. What are three types of asexual reproduction?
2. Define gamete and zygote. What number of chromosomes does each have?
3. What happens during fertilization?
4. Outline the phases of meiosis.
5. What is a life cycle?
6. What is gametogenesis, and when does it occur?

Apply Concepts

7. Create a diagram to show how crossing-over occurs and how it creates new gene combinations on each chromosome.

8. An adult organism produces gametes that quickly go through fertilization and form diploid zygotes. The zygotes mature into adults, which live for many years. Eventually the adults produce gametes and the cycle repeats. What type of life cycle does this organism have? Explain your answer.

Think Critically

9. Compare and contrast asexual and sexual reproduction.
10. Explain why sexual reproduction results in genetically unique offspring.
11. Explain how meiosis I differs from mitosis.

Points to Consider

In sexually reproducing organisms, parents pass a copy of each type of chromosome to their offspring by producing gametes. When gametes are fertilized and form offspring, each has a unique combination of chromosomes and genes from both parents. The inherited gene combination determine the characteristics of the offspring.

- Is it possible to predict possible gene combinations in offspring from the genes of their parents?
- Can the characteristics of offspring be predicted from the characteristics of their parents?

7.2 Lesson 7.1: Mendel's Investigations

Lesson Objectives

- Identify how Mendel's study of science and math was important to his success in research.
- Distinguish between characteristics and traits.
- Explain how Mendel was able to control pollination of the pea plants.
- Identify the terms used to describe the three generations in Mendel's studies.
- State one reason for carrying out a monohybrid cross.
- Identify the traits that appeared in Mendel's F_2 generation.
- Identify the actions of dominant alleles and recessive alleles for a trait.
- Outline the Law of Segregation.
- Outline the Law of Independent Assortment.
- Explain Mendel's results in relation to genes and chromosomes.
- Distinguish between genotype and phenotype.

Introduction

For thousands of years, humans have understood that characteristics such as eye color or flower color are passed from one generation to the next. The passing of characteristics from parent to offspring is called **heredity**. Humans have long been interested in understanding heredity. Many hereditary mechanisms were developed by scholars but were not properly tested or quantified. The scientific study of genetics did not begin until the late 19th century. In experiments with garden peas, Austrian monk Gregor Mendel described the patterns of inheritance.

Gregor Mendel: Teacher and Scientist

Gregor Johann Mendel was an Augustinian monk, a teacher, and a scientist (**Figure** 7.10). He is often called the "father of modern genetics" for his study of the inheritance of traits in pea plants. Mendel showed that the inheritance of traits follows particular laws, which were later named after him. The significance of Mendel's work was not recognized until the turn of the 20th century. The rediscovery of his work led the foundation for the era of modern **genetics**, the branch of biology that focuses on heredity in organisms.

Johann Mendel was born in 1822 and grew up on his parents' farm in an area of Austria that is now in the Czech Republic. He overcame financial hardship and ill health to excel in school. In 1843 he entered the Augustinian Abbey in Brünn (now Brno, Czech Republic.) Upon entering monastic life, he took the name Gregor. While at the monastery, Mendel also attended lectures on the growing of fruit and agriculture at the Brünn Philosophical Institute. In 1849 he accepted a teaching job, but a year later he failed the state teaching examination. One of his examiners recommended that he be sent to university for further studies. In 1851 he was sent to the University of Vienna to study natural science and mathematics. Mendel's time at Vienna was very important in his development as a scientist. His professors encouraged him to learn science through experimentation and to use mathematics to help explain observations of natural events. He returned to Brünn in 1854 as a natural history and physics teacher.

Mendel's Experiments

In 1853 and 1854, Mendal published two papers on crop damage by insects. However, he is best known for his later studies of the pea plant *Pisum sativum.* Mendel was inspired by both his professors at university

Figure 7.10: Gregor Johann Mendel

and his colleagues at the monastery to study variation in plants. He had carried out artificial fertilization on plants many times in order to grow a plant with a new color or seed shape. **Artificial fertilization** is the process of transferring pollen from the male part of the flower to the female part of another flower. Artificial fertilization is done in order to have seeds that will grow into plants that have a desired trait, such as yellow flowers.

During Mendel's time, the popular **blending inheritance** hypothesis stated that offspring were a "mix" of their parents. For example, if a pea plant had one short parent and one tall parent, that pea plant would be of medium height. It was believed that the offspring would then pass on heritable units, or factors, for medium sized offspring. (Today we know these heritable units are genes; however, Mendel did not know of the concept of a gene.) Mendel noted that plants in the monastery gardens sometimes gave rise to plants that were not exactly like the parent plants, nor were they a ‘‘mix” of the parents. He also noted that certain traits reappeared after ‘‘disappearing” in an earlier generation. Mendel was interested in finding out if there was a predictable pattern to the inheritance of traits. Between 1856 and 1863 he grew and tested about 29,000 pea plants in the monastery garden.

Mendel may have chosen to study peas because they are fast-growing plants that are available in different varieties. For example, one variety of pea plant has purple flowers, as shown in **Figure** 7.11, while another variety has white flowers.

Mendel chose to study seven characteristics of pea plants. A **characteristic** is a heritable feature, such as flower color. Each characteristic Mendel chose to study occurred in two contrasting traits. A **trait** is a heritable variant of a characteristic, such as purple or white flower color. Table 7.1 lists the seven characteristics Mendel studied, and their two contrasting traits.

Table 7.1: (continued)

Flower Color	Flower Position on Stem	Stem Length	Pod Shape	Pod Color	Seed Shape	Seed Color

Table 7.1: **The Seven Characteristics Mendel Studied and Their Contrasting Traits**

Flower Color	Flower Position on Stem	Stem Length	Pod Shape	Pod Color	Seed Shape	Seed Color
violet-red (purple)	axial	tall	inflated	green	round	green
white	terminal	short	constricted	yellow	wrinkled	yellow

Pea Plant Pollination

In order to study these characteristics, Mendel needed to control the pollination of the pea plants. Pollination occurs when the pollen from the male reproductive part of a flower, called the anthers, is transferred to the female reproductive part of a flower, called the stigma. Pea plants are **self-pollinating**, which means the pollen from a flower on a single plant transfers to the stigma of the same flower or another flower on the same plant. In order to avoid self-pollination, Mendel removed the anthers from the flowers on a plant. He then carefully transferred pollen from the anthers of another plant and dusted the pollen onto the stamen of the flowers that lacked anthers. This process caused cross-pollination. **Cross-pollination** occurs when pollen from one flower pollinates a flower on a different plant. In this way, Mendel controlled the characteristics that were passed onto the offspring. **Figure** 7.12 shows the location of the male and female parts of *P. sativum.*

Mendel's First Experiment

Mendel began his studies by growing plants that were true-breeding for a particular trait. A **true-breeding** plant will always produce offspring with that trait when they self-pollinate. For example, a true-breeding plant with yellow seeds will always have offspring that have yellow seeds. In his first experiment, Mendel cross-pollinated two true-breeding plants of contrasting traits, such as purple and white flowered plants. The true-breeding parent plants are referred to as the **P generation** (parental generation). The hybrid offspring of the P generation are called the **F_1 generation** (filial generation). The hybrid offspring of the F_1 generation are called the F_2 generation (filial generation).

Monohybrid Crosses

Mendel first worked with plants that differed in a single characteristic, such as flower color. A hybridization is a cross between two individuals that have different traits. A hybridization in which only one characteristic is examined is called a **monohybrid cross**. The offspring of such a cross are called **monohybrids**. Mendel noted that hybridizing true-breeding (P-generation) plants gave rise to an F_1 generation that showed only one trait of a characteristic. For example, a true-breeding purple-flowering plant crossed with a true-breeding white-flowering plant always gave rise to purple-flowered hybrid plants. There were no white-flowered hybrids! Mendel wanted to know what happened to the white-flowered plants' "heritable factors." If indeed the white-flower "heritable factor" had disappeared, all future offspring of the hybrids

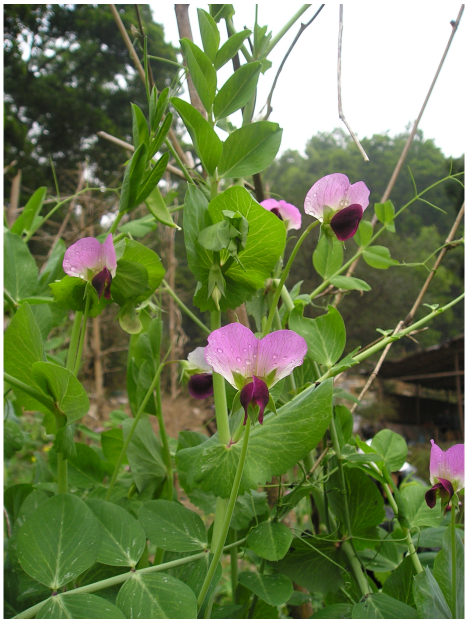


Figure 7.11: the pea plant species that Mendel studied.

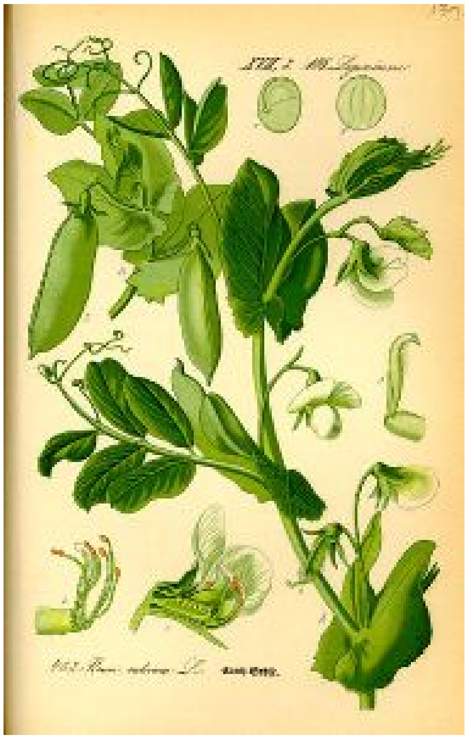


Figure 7.12: The location of the anthers in the pea flower. The anthers are illustrated alone in the image to the left of the transected flower (at right). Mendel controlled pollination of the plants by removing the immature anthers of certain plants.

would be purple-flowered. To test this idea, Mendel let the F_1 generation plants self-pollinate and then planted the resulting seeds.

Mendel's Results

The F_2 generation plants that grew included white-flowered plants! Mendel noted the ratio of white flowered plants to purple-flowered plants was about 3:1. That is, for every three purple-flowered plants, there was one white flowered plant. **Figure** 7.13 shows Mendel's results for the characteristic of flower color.

Mendel carried out identical studies over three generations, (P, F_1, and F_2), for the other six characteristics and found in each case that one trait "disappeared" in the F_1 generation, only to reappear in the F_2 generation. Mendel studied a large number of plants, as shown in **Table** 7.2, so he was confident that the ratios of different traits in the F_2 generation were representative.

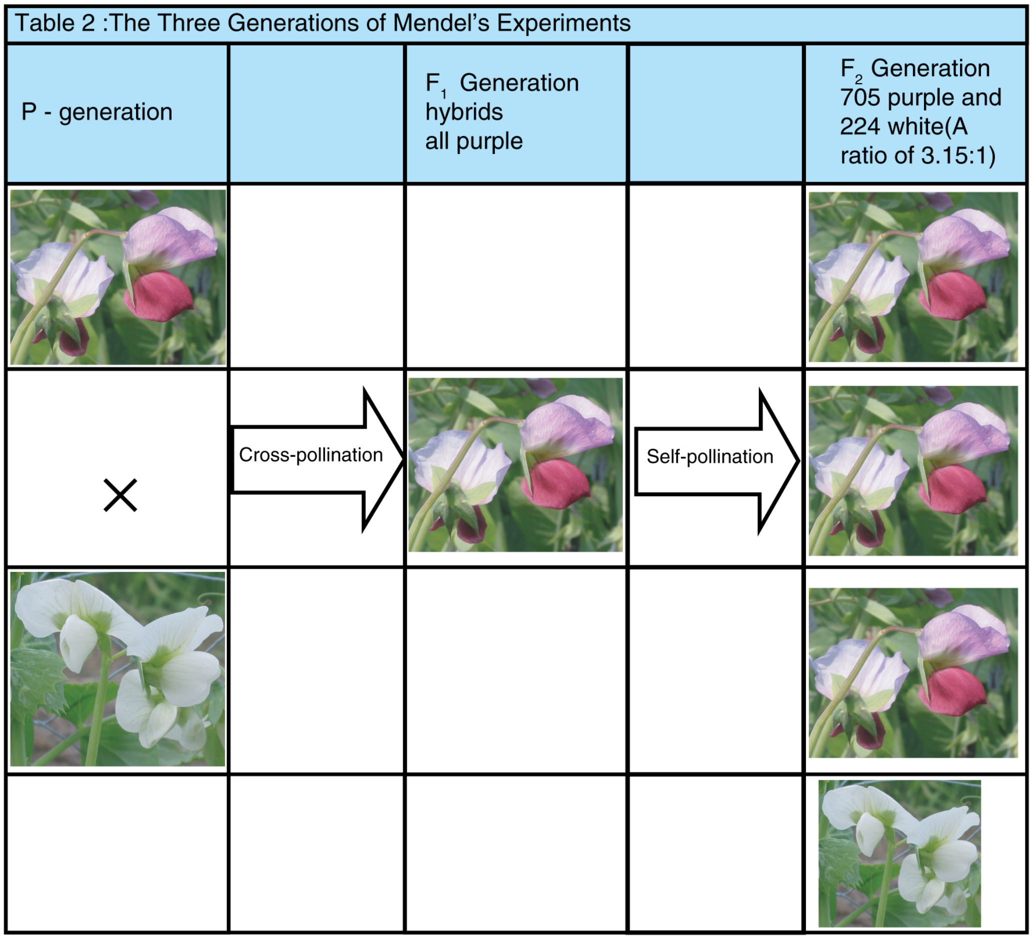


Table 2 :The Three Generations of Mendel's Experiments

P - generation		F_1 Generation hybrids all purple		F_2 Generation 705 purple and 224 white(A ratio of 3.15:1)
×	Cross-pollination		Self-pollination	

Figure 7.13

Table 7.2: **Results of F1 Generation Crosses for Seven Characteristics in *P. sativum***

Characteristic	Dominant Trait	Recessive Trait	F2 Generation Dominant:Recessive	Ratio
Flower color	Purple	White	705:224	3.15:1
Flower position on stem	Axial	Terminal	651:207	3.14:1
Stem length	Tall	Short	787:277	2.84:1
Pod shape	Inflated	Constricted	882:299	2.95:1
Pod color	Green	Yellow	428:152	2.82:1
Seed shape	Round	Wrinkled or angular	5474:1850	2.96:1
Seed color	Yellow	Green	6022:2001	3.01:1

Mendel's Theory of Heredity

Based on his observations, Mendel developed four hypotheses. These hypotheses are known as Mendel's theory of heredity. The hypotheses explain a simple form of inheritance in which two alleles of a gene are inherited to result in one of several traits in offspring. In modern terms, these hypotheses are:

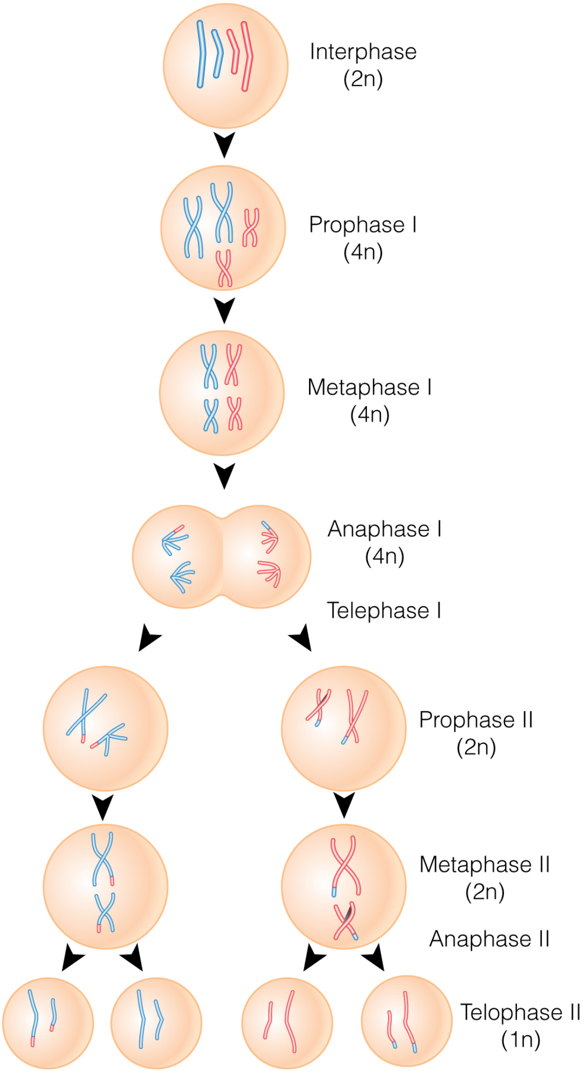
1. **There are different versions of genes**. These different versions account for variations in characteristics. Different versions of a gene are called **alleles.** For example, there is a ‘‘yellow-pod” allele and a ‘‘green pod” allele. The blending inheritance hypothesis was discredited by Mendel's allele hypothesis.
2. **When two different alleles are inherited together, one may be expressed, while the effect of the other may be ‘‘silenced.”** In the case of pod color, the allele for green pods is always expressed and is **dominant**. The allele for yellow pods, which is not expressed, is **recessive**. For instance, if a plant inherits a ‘‘yellow-pod” gene and a ‘‘green pod” gene, it will have only green pods.
3. **For each characteristic, an organism inherits two alleles, one from each parent**. Mendel noted that offspring could inherit their traits from either parent. In the case of the expressed trait, it did not matter whether it was the male gamete or female gamete that supplied the gene.
4. **When gametes are formed, the two alleles of each gene are separated** (**Figure** 7.14). During meiosis, each male or female gamete receives one allele for a trait. When the male and female gametes are fused at fertilization, the resulting zygote contains two alleles of each gene.

Random Segregation of Alleles

The **Law of Segregation** states that a pair of alleles is separated, or segregated, during the formation of gametes. During meiosis, homologous chromosomes are randomly separated. Each resulting gamete has an equal probability or chance of receiving either of the two alleles.

Mendel's Second Experiment

Mendel also crossed pea plants that differed in two characteristics, such as seed color and shape. A **dihybrid cross** is a cross in which the inheritance of two characteristics are tracked at the same time.



Parent Cell

Homologous chromosomes separate during Anaphase I and sister chromatids stay together.

Sister chromatids separate and four daughter cells (gametes) result. Each gamete has an equal chance of receiving any one of a pair of alleles.

Figure 7.14: Alleles on homologous chromosomes are randomly separated during gamete formation. Upon fertilization, the fusion of a male and female gametes results in new combinations of alleles in the resulting zygote.

The offspring of such a cross are called **dihybrids**. Mendel wanted to see if the inheritance of characteristics were dependent. He concluded that characteristics were inherited independently of each other.

The Law of Independent Assortment

The **Law of Independent Assortment**, also known as or Mendel's Second Law, states that the inheritance of one trait will not affect the inheritance of another. Mendel concluded that different traits are inherited independently of each other, so that there is no relationship, for example, between seed color and seed shape. In modern terms, alleles of each gene separate independently during gamete formation.

Linked Genes on Chromosomes

We now know that the only alleles that are inherited independently are ones that are located far apart on a chromosome or that are on different chromosomes. There are many genes that are close together on a chromosome, and are packaged into the gametes together. Genes that are inherited in this way are called **linked genes**. Linked genes tend to be inherited together because they are located on the same chromosome. Genetic linkage was first discovered by the British geneticists William Bateson and Reginald Punnett shortly after Mendel's laws were rediscovered.

Mendelian Theory and Molecular Genetics

Mendel was perhaps lucky in that the characteristics he chose to study in the pea plants had a relatively simple pattern of inheritance. These characteristics were determined by one gene for which there were exactly two alleles. One of these alleles was dominant and the other recessive. Had any of these characteristics been determined by more than one gene, he may not have been able to develop such amazing insight into inheritance. In many instances, the relationship between genes and inheritance is more complex than that which Mendel found. Nevertheless, geneticists have since found that Mendel's findings can be applied to many organisms. For example, there are clear patterns of Mendelian inheritance in humans. Albinism (**Figure** 7.15), is a genetic disorder that is inherited as a simple Mendelian trait.

Dominant and Recessive Alleles

Mendel used letters to represent dominant and recessive factors. Likewise, geneticists now use letters to represent alleles. Capital letters refer to dominant alleles, and lowercase letters refer to recessive alleles. For example, the dominant allele for the trait of green pod color is indicated by G. The recessive trait of yellow pod color is indicated by g. A true-breeding plant for green pod color would have identical alleles GG in all its somatic cells. Likewise, a true-breeding plant for yellow pod color would have identical alleles gg in all of its somatic cells. During gamete formation, each gamete receives one copy of an allele. When fertilization occurs between these plants, the offspring receives two copies of the allele, one from each parent. In this case, all of the offspring would have two different alleles, Gg, one from each of its parents.

An organism that has an identical pair of alleles for a trait is called **homozygous**. The true-breeding parents GG and gg are homozygous for the pod color gene. Organisms that have two different alleles for a gene are called **heterozygous**. The offspring of the cross between the GG and gg plants are all heterozygous for the pod color gene. Due to dominance and recessiveness of alleles, an organism's traits do not always reveal its genetics. Therefore, geneticists distinguish between an organism's genetic makeup, called its **genotype**, and its physical traits, called its **phenotype**. For example, the GG parent and the Gg offspring have the same phenotype (green pods) but different genotypes.

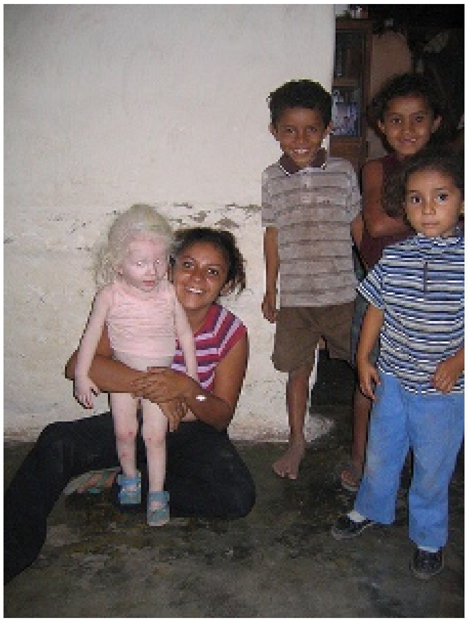


Figure 7.15: Albinism is a recessively inherited disorder in which the body does not produce enough of the pigment melanin. The skin, hair, and eyes of a person with albinism appear white or pale.

Lesson Summary

- Genetics is the branch of biology that focuses on heredity in organisms.
- Modern genetics is based on Mendel's explanation of how traits are passed from generation to generation.
- Mendel's use of mathematics in his pea plant studies was important to the confidence he had in his results.
- Mendel carried out his first experiments with true-breeding plants and continued them over a span of three generations.
- For each of the seven characteristics Mendel studied, he observed a similar ratio in the inheritance of dominant to recessive traits (3:1) in the F_2 generation.
- Mendel developed a theory that explained simple patterns of inheritance in which two alleles are inherited to result in one of several traits in offspring.
- The law of segregation states that a pair of alleles is segregated during the formation of gametes and that each gamete has an equal chance of getting either one of the allele.
- The law of independent assortment states that the inheritance of one trait will not affect the inheritance of another. That is, genes are inherited independently of each other.
- Linked genes are genes that are close together on the same chromosome. Linked genes are inherited together.
- Mendelian inheritance patterns can be seen in humans. Albinism is a genetic disorder that is inherited as a simple Mendelian trait.
- Genotype determines phenotype. A homozygous dominant or a heterozygous genotype will always show a dominant phenotype. A homozygous recessive genotype can only show a recessive phenotype.

Review Questions

1. Why was Mendel's understanding of mathematics and science important for his research?
2. What did Gregor Mendel contribute to the science of genetics?

3. What is a true-breeding plant?
4. How was Mendel able to control the pollination of his pea plants?
5. How does cross-pollination differ from self-pollination?
6. How did the appearance of Mendel's F_1 generation differ from the appearance of the P generation?
7. Identify the relationship between genes and alleles.
8. Summarize the law of segregation.
9. Summarize the law of independent assortment.
10. Relate the term homozygous to heterozygous by using an example from Mendel's experiments.
11. Relate the term genotype to phenotype by using an example from Mendel's experiments.
12. Why can't you always identify the genotype of an organism from its phenotype?

Further Reading / Supplemental Links

- http://www.mendelweb.org/MWtime.html
- http://www.umn.edu/ships/updates/mendel.htm
- http://www.macalester.edu/psychology/whathap/UBNRP/visionwebsite04/twotypes.html
- http://www.mendelweb.org
- http://www.umn.edu/ships/updates/mendel2.htm
- http://anthro.palomar.edu/mendel/mendel_1.htm
- http://www.mendel-museum.org/eng/1online/experiment.html
- http://evolution.berkeley.edu/evosite/history/discretegenes.shtml
- http://en.wikipedia.org

Vocabulary

allele Different versions of a gene.

anther The male reproductive part of a flower.

artificial fertilization The process of transferring pollen from the male part of the flower to the female part of another flower; done in order to have seeds that will grow into plants that have a desired trait.

blending inheritance hypothesis Hypothesis that stated that offspring were a ”mix” of their parents.

characteristic A heritable feature, such as flower color.

cross-pollination Fertilization in which pollen from one flower pollinates a flower on a different plant.

dihybrid cross A cross in which the inheritance of two characteristics are tracked at the same time.

dominant The allele that is expressed when two separate alleles are inherited.

F_1 generation The hybrid offspring of the P (parental) generation; first filial generation.

genetics The branch of biology that focuses on heredity in organisms.

genotype An organism's genetic makeup.

heredity The passing of characteristics from parent to offspring.

heterozygous Organisms that have two different alleles for a gene.

homozygous An organism that has an identical pair of alleles for a trait.

hybridization A cross between two individuals that have different traits.

Law of Independent Assortment States that the inheritance of one trait will not affect the inheritance of another.

Law of Segregation States that a pair of alleles is separated, or segregated, during the formation of gametes.

linked genes Genes that are close together on a chromosome, and are packaged into the gametes together.

monohybrid cross A hybridization in which only one characteristic is examined.

phenotype An organism's physical traits.

recessive The allele that is expressed only in the absence of a dominant allele.

self-pollinating Fertilization in which the pollen from a flower on a single plant transfers to the stigma of the same flower or another flower on the same plant.

stigma The female reproductive part of a flower.

trait A heritable variant of a characteristic, such as purple or white flower color.

true-breeding A plant that will always produce offspring with the parental trait when it self-pollinates.

Points to Consider

Next we will examine Mendelian Inheritance in further detail.

- Do you think all inheritance is as straightforward as the inheritance in pea plants?
- Is there a relationship between inheritance and probability? What might that relationship be?

7.3 Lesson 7.2: Mendelian Inheritance

Lesson Objectives

- Identify how probability is used to predict outcomes of genetic crosses.
- Outline how a Punnett Square helps predict outcomes of genetic crosses.
- Identify how probability can help determine the alleles in a gamete.
- Identify how a testcross is used to determine the genotype of an organism.
- Describe how monohybrid and dihybrid crosses differ.
- Identify the ratio of phenotypes that appeared in Mendel's dihybrid crosses.
- Examine how a pedigree is used in the study of human inheritance.
- Describe how codominance does not follow Mendelian Inheritance.
- Describe how incomplete dominance does not follow Mendelian Inheritance.
- Identify examples of polygenic traits in humans.
- Outline how heredity and environment can interact to affect phenotype.

Introduction

A **Mendelian trait** is a trait that is controlled by a single gene that has two alleles. One of these alleles is dominant and the other is recessive. Several inheritable conditions in humans are passed to offspring in a simple Mendelian fashion. Medical professionals use Mendel's laws to predict and understand the inheritance of certain traits in their patients. Also, farmers, animal breeders, and horticulturists who breed organisms can predict outcomes of crosses by understanding Mendelian inheritance.

Calculating Probability

The rules of probability that apply to tossing a coin or throwing a dice also apply to the laws of segregation and independent assortment. **Probability** is the likelihood that a certain event will occur. It is expressed by comparing the number of events that occur to the total number of possible events. The equation is written as:

Probability = (number of times an event is expected to occur/total number of times an event could happen)

For example, in Mendel's F_2 hybrid generation, the dominant trait of purple flower color appeared 705 times, and the recessive trait appeared 224 times. The dominant allele appeared 705 times out of a possible 929 times (705+224=929).

Probability = (705/929)

(705/929)= 0.76

Probability is normally expressed in a range between 0 and 1, but it can also be expressed as a percentage, fraction, or ratio. Expressed as a percentage, the probability that a plant of the F_2 generation will have purple flowers is 76%. Expressed as a fraction it is about &frac;34;,and as a ratio it is roughly 3:1. The probability of the expression of the dominant allele for other characteristics can also be calculated the same way. In fact, Mendel found that all the other dominant "factors" had approximately a &frac;34; probability of being expressed in the F_2 hybrid generation. Review Table 7.1 for the results for the other six characteristics.

The probability the recessive trait will appear in the F_2 hybrid generation is calculated in the same way.

Probability = (224/929)

(224/929) = 0.24

The probability of the recessive trait appearing in the F_2 generation is 24% or about &frac;14;.

Results predicted by probability are most accurate when many trials are done. The best way to illustrate this idea is to toss a coin. Because a coin has two sides, every time you toss it the chance of tossing heads or tossing tails is 50%. The outcome of each separate toss is unaffected by any previous or future result. For example, imagine you tossed seven heads in a row. You would think that the next toss is more likely to be a tail, but the possibility of tossing another head is still 50%. If you tossed the coin a total of ten times, a total of seven heads and three tails, you would calculate the probability of tossing heads is 70%. The fact that you carried out only a small number of trials has affected your results. If Mendel had grown only 10 plants, he would have gotten different probabilities for the appearance of dominant and recessive traits. However, Mendel carried out many thousands of trials. He was therefore sure that his results were due to probability, and not to chance.

Probability and the Law of Segregation

Each coin toss is a separate event. Likewise, gamete formation is a separate event. The probability that a Pp heterozygote produces gametes with a P allele or a p allele is 50% for each gamete cell. In a fertilization involving two such plants (as in the F_1 generation self-pollination experiment), each pollen cell and each egg cell have a 50% chance of having the P or p allele.

Predicting Genotypes with Punnett Squares

Mendel developed the law of segregation by following only a single characteristic, such as pod color, in his pea plants. Biologists use a diagram called a **Punnett Square**, to help predict the probable inheritance of alleles in different crosses. In a monohybrid cross, such as the one in **Figure** 7.16, the Punnett square shows every possible combination when combining one maternal (mother) allele with one paternal (father) allele. In this example, both organisms are heterozygous for flower color Pp (purple). Both plants produce gametes that contain both the P and p alleles. The probability of any single offspring showing the dominant trait is 3:1, or 75%.

Using Probability to Determine Alleles in Gametes

In the monohybrid cross shown in **Figure** 7.16, two heterozygous plants are crossed. Both plants produce gametes, all of which contain either a P or p allele for flower color. The likelihood that any particular gamete contains the allele for a white flower can be calculated. Because a gamete can only carry one out of two alleles, there are only two possible outcomes for a gamete. The probability that a gamete will carry the allele for white flower color is &frac;12;, 0.5, or 50%. The probability that a gamete will carry the allele for purple flower color is also &frac;12;.

Using Probability in a Heterozygous Cross

We can calculate the probability of any one of the offspring being heterozygous (Pp) or homozygous (PP or pp) for flower color. The probability of a plant inheriting the P or p allele from a heterozygous parent is &frac;12;. Multiply the probabilities of inheriting both alleles to find the probability that any one plant will be a pp homozygote.

&frac;12; × &frac;12; = &frac;14; or 0.25

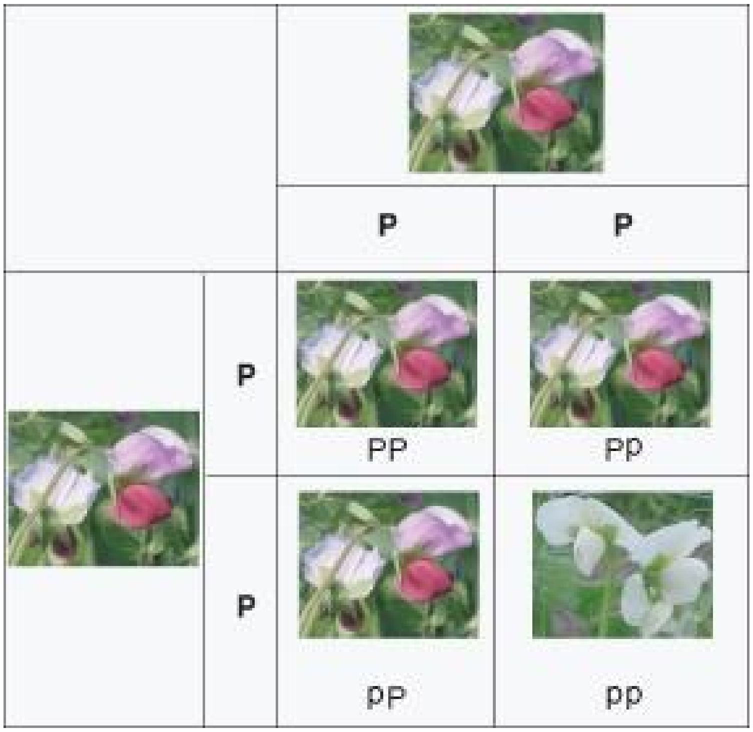


Figure 7.16: A Punnett square helps determine the genotype of this heterozygous cross. Two pea plants, both heterozygous for flower color, are crossed. The offspring will show the dominant purple coloration in a 3:1 ratio. Or, about 75% of the offspring will be purple.

Only 25 %, or one outcome out of four, will result in a plant homozygous for white flower color (pp). The possibility that any one plant will be a PP homozygote is also 1/4. The heterozygous allele combination can happen twice (Pp or pP), so the two probabilities are added together &frac;14; + &frac;14; = 2/4, or &frac;12;. The probability that an offspring plant will be Pp heterozygous is &frac;12;.

Testcross and Punnett Squares

Suppose you have a purple and white flower and, as discussed above, purple color is dominant to white. The white flower must be homozygous for the recessive allele, but the genotype of the purple flower is unknown. It could be either PP or Pp. A testcross will determine the organism's genotype. In a **testcross**, the individual with the unknown genotype is crossed with a homozygous recessive individual (**Figure** 7.17). The unknown genotype can be determined by observing the phenotypes of the resulting offspring.

Dihybrid Crosses and Punnett Squares

Dihybrid crosses are more complicated than monohybrid crosses because more combinations of alleles are possible. For example, tracking the inheritance of seed color and pod color in a Punnett square requires that we track four alleles. G is the dominant allele for green pod color and g is the recessive allele for yellow pods. Y is the dominant allele for yellow seed color and y is the recessive allele for green seed color.

Two plants are crossed, one is true-breeding for green pods and yellow seeds (GGYY), the other is true-breeding for yellow pods and green seeds (ggyy). All of the F_1 generation will be heterozygous for both traits (GgYy). **Figure** 7.18, shows the dihybrid cross of the dihybrid P generation and the F_1 generation.

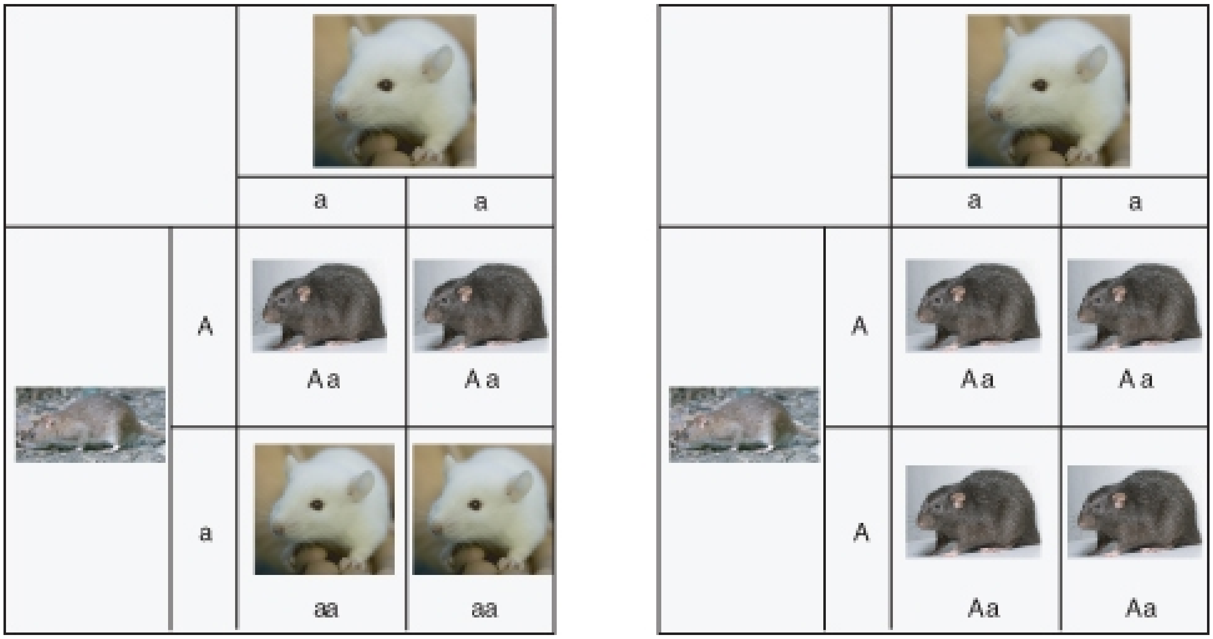


Figure 7.17: A testcross helps reveal the genotype of an organism when that organism shows the dominant trait, such as agouti coat color in rats. Such an organism could be homozygous dominant or heterozygous. Agouti is the common color of the Norway rat,

Heterozygous Dihybrid Cross

In a dihybrid cross, four alleles can be inherited from any one parent at one time. When two heterozygous individuals are crossed, there are a total of 16 possible combinations of the four alleles. The phenotypes of the offspring with two independent traits show a 9:3:3:1 ratio. In a cross involving pea plants heterozygous for round, yellow seeds (GgYy), 9/16 plants have round, yellow seeds, 3/16 have round, green seeds, 3/16 have wrinkled, yellow seeds, and 1/16 has wrinkled, green seeds.

Mendelian Inheritance in Humans

A **pedigree** is a chart which shows the inheritance of a trait over several generations. A pedigree is commonly created for families, and it outlines the inheritance patterns of genetic disorders. **Figure** 7.19 shows a pedigree depicting recessive inheritance of a disorder through three generations. Scientists can tell the genetics of inheritance from studying a pedigree, such as whether the trait is sex-linked (on the X or Y chromosome) or autosomal (on a chromosome that does not determine sex), whether the trait is inherited in a dominant or recessive fashion, and possibly whether individuals with the trait are heterozygous or homozygous.

Is the trait sex-linked or autosomal? A **sex chromosome** is a chromosome that determines the sex of an organism. Humans have two sex chromosomes, X and Y. Females have two X chromosomes (XX), and males have one X and one Y (XY). An **autosome** is any chromosome other than a sex chromosome. If a trait is autosomal it will affect males and females equally.

A **sex-linked trait** is a trait whose allele is found on a sex chromosome. The human X chromosome is significantly larger than the Y chromosome; there are many more genes located on the X chromosome than there are on the Y chromosome. As a result there are many more X-linked traits than there are Y-linked traits. Most sex-linked traits are recessive. Because males carry only one X chromosome, if they inherit a

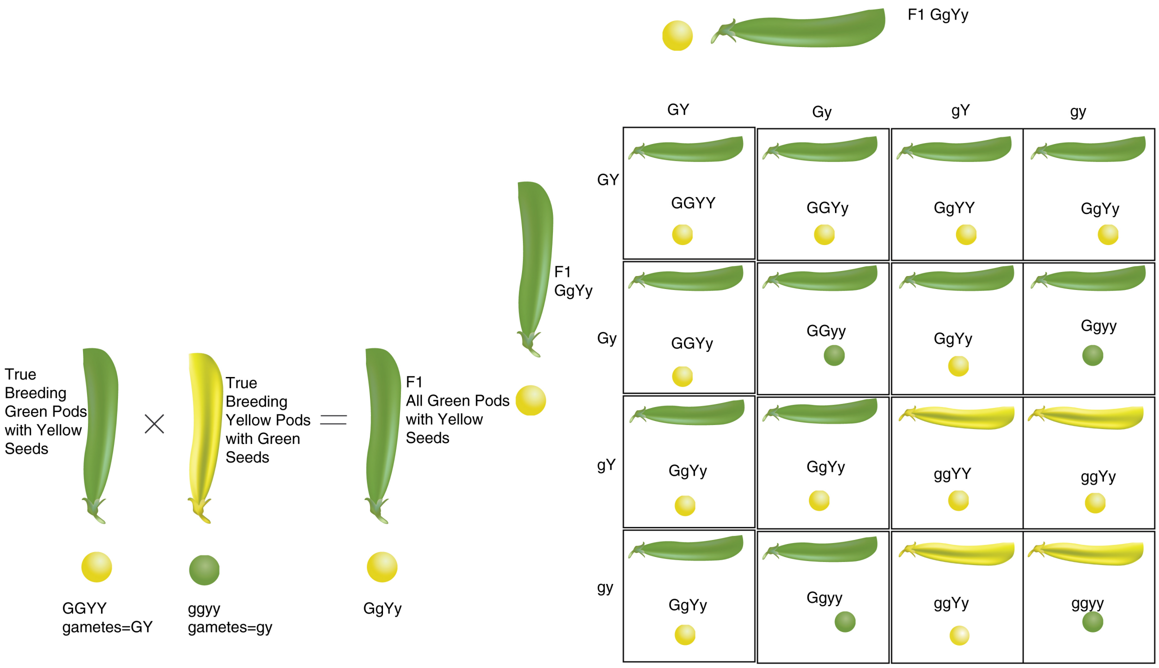


Figure 7.18: The dihybrid crosses were started by crossing two true-breeding plants, just as the monohybrid crosses were. The ratio of phenotypes (9:3:3:1) can be determined from the dihybrid Punnett square on the right. The genotype of the F

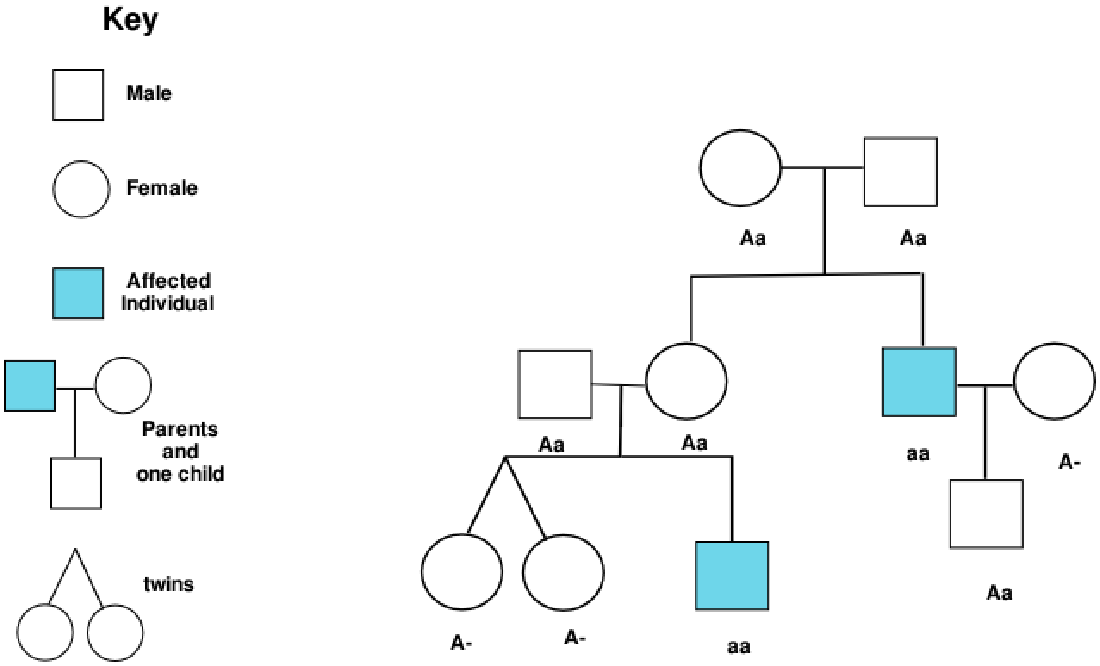


Figure 7.19: In a pedigree, squares symbolize males, and circles represent females. A horizontal line joining a male and female indicates that the couple had offspring. Vertical lines indicate offspring which are listed left to right, in order of birth. Shading of the circle or square indicates an individual who has the trait being traced. The inheritance of the recessive trait is being traced. A is the dominant allele and a is recessive.

recessive sex-linked gene they will show a sex-linked condition.

Because of the recessive nature of most sex-linked traits, a female who shows a sex-linked condition would have to have two copies of the sex-linked allele, one on each of her X chromosomes. **Figure** 7.20 shows how red-green colorblindness, a sex-linked disorder, is passed from parent to offspring.

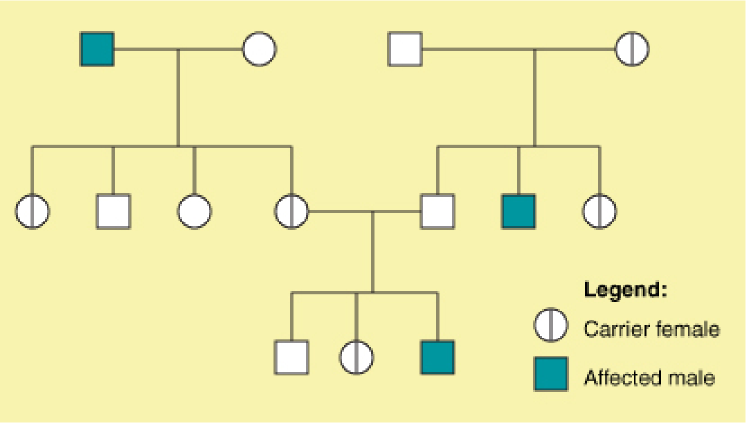


Figure 7.20: An X-linked disorder such as red-green colorblindness is normally passed onto the son of a carrier mother. Usually, females are unaffected as they have a second, normal copy of the allele on the second X chromosome. However, if a female inherits two defective copies of the allele, she will be colorblind. Therefore, every son of a colorblind woman will be colorblind.

Is the Trait Dominant or Recessive? If the trait is autosomal dominant, every person with the trait will have a parent with the trait. If the trait is recessive, a person with the trait may have one, both or neither parent with the trait. An example of an autosomal dominant disorder in humans is Huntington's disease (HD). Huntington's disease is a degenerative disease of the nervous system. It has no obvious effect on phenotype until the person is aged 35 to 45 years old. The disease is non-curable and, eventually, fatal. Every child born to a person who develops HD has a 50% chance of inheriting the defective allele from the parent.

Are the Individuals with the Trait Heterozygous or Homozygous? If a person is homozygous or heterozygous for the dominant allele of a trait, they will have that trait. If the person is heterozygous for a recessive allele of the trait, they will not show the trait. A person who is heterozygous for a recessive allele of a trait is called a **carrier**. Only people who are homozygous for a recessive allele of a trait will have the trait.

Non-Mendelian Modes of Inheritance

The relationship between genotype and phenotype is rarely as simple as the examples Mendel studied. Each characteristic he studied had two alleles, one of which was completely dominant and the other completely recessive. Geneticists now know that alleles can be codominant, or incompletely dominant.

Codominance

Codominance occurs when both traits appear in a heterozygous offspring. Neither allele is completely dominant nor completely recessive. For example, roan shorthorn cattle have codominant genes for hair color. The coat has both red and white hairs. The letter R indicates red hair color, and R' white hair color. In cases of codominance, the genotype of the organism can be determined from its phenotype. The heifer in **Figure** 7.21 is RR' heterozygous for coat color.

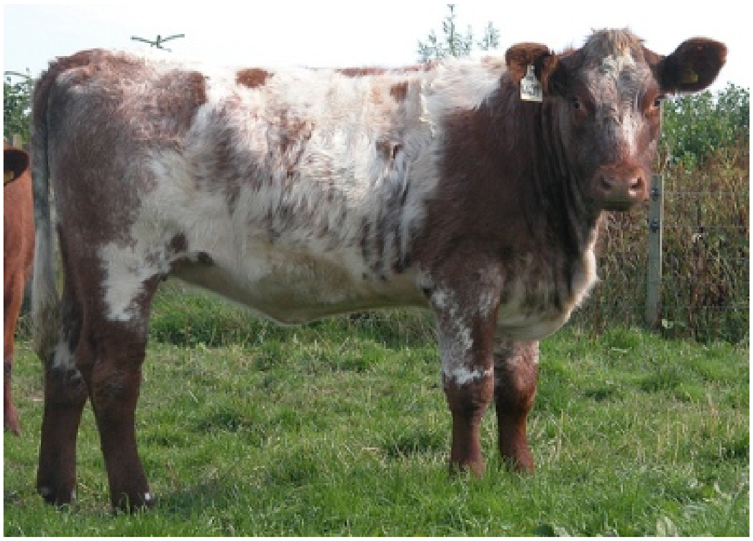


Figure 7.21: The roan coat of this shorthorn heifer is made up of red and white hairs. Both the red and white hair alleles are codominant. Therefore cattle with a roan coat are heterozygous for coat color (RR

Incomplete Dominance

Incomplete dominance occurs when the phenotype of the offspring is somewhere in between the phenotypes of both parents; a completely dominant allele does not occur. For example, when red snapdragons (C^RC^R)</math> are crossed with white snapdragons (C^WC^W), the F_1 hybrids are all pink hetrozygotes for flower color (C^RC^W). The pink color is an intermediate between the two parent colors. When two F_1 (C^RC^W) hybrids are crossed they will produce red, pink, and white flowers. The genotype of an organism with incomplete dominance can be determined from its phenotype (**Figure** 7.22).

		White Flower	
		C^W	C^W
Red Flower	C^R	C^RC^W	C^RC^W
	C^R	C^RC^W	C^RC^W

Figure 7.22: Snapdragons show incomplete dominance in the traits for flower color. The offspring of homozygous red-flowered and homozygous white-flowered parents are heterozygous pink-flowered.

Complex Forms of Heredity

Traits that are affected by more than one gene are called **polygenic traits**. The genes that affect a polygenic trait may be closely linked on a chromosome, unlinked on a chromosome, or on different chromosomes. Polygenic traits are often difficult for geneticists to track because the polygenic trait may have many alleles. Also, independent assortment ensures the genes combine differently in gametes. Therefore, many different intermediate phenotypes exist in offspring. Eye color (**Figure** 7.23), and skin color are examples of polygenic traits in humans.

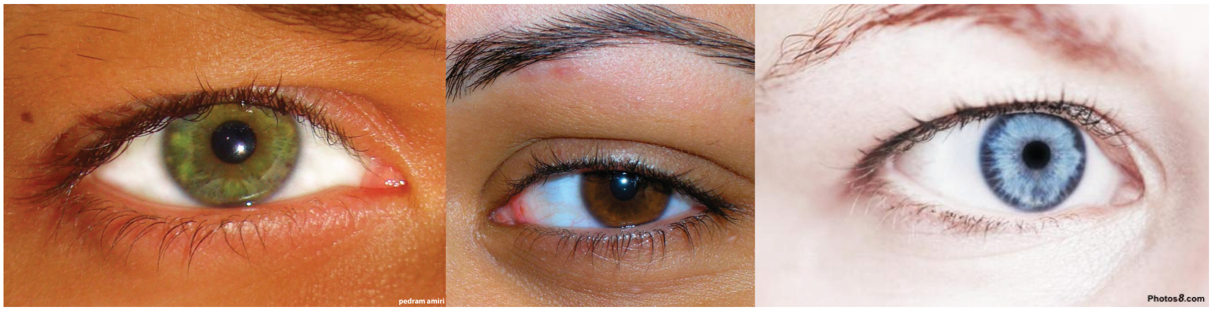


Figure 7.23: Eye color and skin color are examples of polygenic traits; they are influenced by more than one gene.

When three or more alleles determine a trait, the trait is said to have **multiple alleles**. The human ABO blood group is controlled by a single gene with three alleles: i, I^A, I^B, and the recessive i allele. The gene encodes an enzyme that affects carbohydrates that are found on the surface of the red blood cell. A and B refer to two carbohydrates found on the surface of red blood cells. There is not an O carbohydrate. Type O red blood cells do not have either type A or B carbohydrates on their surface.

The alleles I^A and I^B are dominant over i. A person who is homozygous recessive ii has type O blood. Homozygous dominant I^AI^A or heterozygous dominant I^Ai have type A blood, and homozygous dominant I^BI^B or heterozygous dominant I^Bi have type B blood. I^AI^B people have type AB blood, because the A and B alleles are codominant. Type A and type B parents can have a type AB child. Type A and a type B parent can also have a child with Type O blood, if they are both heterozygous (I^Bi,I^Ai). The table (7.3) shows how the different combinations of the blood group alleles can produce the four blood groups, A, AB, B, and O.

Table 7.3: **Bloodtype as Determined by Multiple Alleles**

	I^A	**I^B**	**i**
I^A	I^AI^A TYPE A	I^AI^B TYPE AB	I^Ai TYPE A
I^B	I^A I^B TYPE AB	I^B I^B TYPE B	I^B i TYPE B
i	i I^A TYPE A	i I^B TYPE B	ii TYPE O

Effects of Environment on Phenotype

Genes play an important part in influencing phenotype, but genes are not the only influence. Environmental conditions, such as temperature and availability of nutrients can affect phenotypes. For example, temperature affects coat color in Siamese cats.

The pointed pattern is a form of partial albinism, which results from a mutation in an enzyme that is

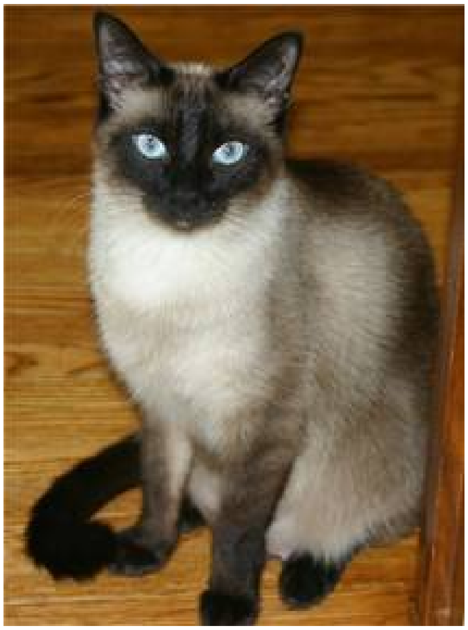


Figure 7.24: The dark

involved in melanin production. The mutated enzyme is heat-sensitive; it fails to work at normal body temperatures. However, it is active in cooler areas of the skin. This results in dark coloration in the coolest parts of the cat's body, such as the lower limbs and the face, as shown in **Figure** 7.24. The cat's face is cooled by the passage of air through the nose. Generally adult Siamese cats living in warm climates have lighter coats than those in cooler climates.

Height in humans is influenced by many genes, but is also influenced by nutrition. A person who eats a diet poor in nutrients will not grow as tall as they would have had they eaten a more nutritious diet. Scientists often study the effects of environment on phenotype by studying identical twins. Identical twins have the same genes, so phenotypic differences between twins often have an environmental cause.

Lesson Summary

- Probability is the likelihood that a certain event will occur. It is expressed by comparing the number of events that actually occur to the total number of possible events. Probability can be expressed as a fraction, decimal, or ratio.
- A Punnett square shows all the possible genotypes that can result from a given cross.
- A testcross examines the genotype of an organism that shows the dominant phenotype for a given trait. The heterozygous organism is crossed with an organism that is homozygous recessive for the same trait.
- A dihybrid cross-examines the inheritance of two traits at the same time.
- A pedigree can help geneticists discover if a trait is sex-linked, if it is dominant or recessive, and if the person (or people) who have the trait are homozygous or heterozygous for that trait.
- The Mendelian pattern of inheritance and expression does not apply to all traits. Codominant traits, incompletely dominant traits, and polygenic traits do not follow simple Mendelian patterns of inheritance. Their inheritance patterns are more complex.
- An organism's phenotype can be influenced by environmental conditions.

Review Questions

1. What does the probability equation help to determine?
2. How can probability be expressed?
3. Outline how Punnett squares are useful.
4. Identify the purpose of a testcross.
5. How do the Punnett squares for a monohybrid cross and a dihybrid cross differ?
6. Mendel carried out a dihybrid cross to examine the inheritance of the characteristics for seed color and seed shape. The dominant allele for yellow seed color is Y, and the recessive allele for green color is y. The dominant allele for round seeds is R, and the recessive allele for a wrinkled shape is r. The two plants that were crossed were F1 dihybrids RrYy. Identify the ratios of traits that Mendel observed in the F2 generation, and explain in terms of genotype what each number means. Create a Punnett square to help you answer the question.
7. Draw a pedigree that illustrates the passing of the dominant cleft chin trait through three generations. A person who has two recessive alleles does not have a cleft chin. Let us say that C is the dominant allele, c is the recessive allele.
8. A classmate tells you that a person can have type AO blood. Do you agree? Explain.
9. Mendelian inheritance does not apply to the inheritance of alleles that result in incomplete dominance and codominance. Explain why this is so.
10. Outline the relationship between environment and phenotype.

Further Reading / Supplemental Links

- http://www.nbii.gov/portal/server.pt?open=512&#38;amp;objID=405&#38;amp;PageID=581&#38;amp;mod
  hi_userid=2&#38;amp;cached=true
- http://omia.angis.org.au/retrieve.shtml?pid=417
- http://www.curiosityrats.com/genetics.html
- http://www.macalester.edu/psychology/whathap/UBNRP/visionwebsite04/twotypes.html
- http://www.nlm.nih.gov/
- http://www.newton.dep.anl.gov/askasci/mole00/mole00087.htm
- http://www.hhmi.org/biointeractive/vlabs/cardiology/content/dtg/pedigree/pedigree.html
- http://www.ndsu.nodak.edu/instruct/mcclean/plsc431/mendel/mendel9.htm
- http://www.emc.maricopa.edu/faculty/farabee/BIOBK/BioBookgeninteract.html

Vocabulary

autosome Any chromosome other than a sex chromosome.

carrier A person who is heterozygous for a recessive allele of a trait.

codominance Occurs when both traits appear in a heterozygous individual.

incomplete dominance Occurs when the phenotype of the offspring is somewhere in between the phenotypes of both parents; a completely dominant allele does not occur.

Mendelian trait A trait that is controlled by a single gene that has two alleles.

multiple alleles When three or more alleles determine a trait, such as with the human ABO blood group.

probability The likelihood that a certain event will occur.

pedigree A chart which shows the inheritance of a trait over several generations.

polygenic traits Traits that are affected by more than one gene.

Punnett square A diagram that helps predict the probable inheritance of alleles in different crosses.

sex chromosome A chromosome that determines the sex of an organism.

sex-linked trait A trait whose allele is found on a sex chromosome.

testcross A cross used to determine an unknown genotype.

Points to Consider

The next chapter is *Molecular Genetics.*

- What do you think Molecular Genetics refers to?
- How can DNA contain all the genetic information?
- If DNA is in the nucleus, and proteins are made on ribosomes in the cytoplasm, how do you think this happens?

Chapter 8

Human Genetics

8.1 Human Chromosomes and Genes

Lesson Objectives

- What is a genetic disease?
- What is the human genome?
- Discuss the importance of characterizing the human genome.
- Define autosome and sex-chromosome.
- Discuss the importance of SNPs.
- What is a karyotype?
- Define sex-linked and X-inactivation.

Introduction

As has been previously discussed, genetics is the branch of biology that focuses on heredity. The basics of heredity are similar for all organisms that reproduce sexually: the offspring receive one set of genetic material from one parent and the other set from the other parent. But are there aspects of genetics that are specific for us? Let's find out.

A **genetic disease** is a phenotype due to a mutation in a gene or chromosome. Many of these mutations are present at conception and are therefore in every cell of the body. Mutant alleles may be inherited from one or both parents, resulting in a dominant or recessive hereditary disease. Currently, there are over 4,000 known genetic disorders, with many more phenotypes yet to be identified. Theoretically, every human gene, when disrupted due to a mutation, could result in at least one disease-type phenotype. Genetic diseases are typically diagnosed and treated by a **geneticist**, a medical doctor specializing in these disorders, many of which are extremely rare and difficult to diagnose. Individuals and families with genetic diseases, or suspected genetic diseases, are often counseled by **genetic counselors**, individuals trained in human genetics and counseling. To understand human genetic diseases, you first need to understand human chromosomes and genes.

The Human Genome

What makes each one of us unique? You could argue that the environment plays a role, and it does to some extent. But most would agree that your parents have something to do with your uniqueness. In fact, it is our genes that make each one of us unique – or at least genetically unique. We all have the genes that make us human: the genes for skin and bones, eyes and ears, fingers and toes, and so on. However, we all have different skin colors, different bone sizes, different eye colors and different ear shapes. In fact, even though we have the same genes, the products of these genes work a little differently in most of us. And that is what makes us unique.

The human genome is the genome - all the DNA - of *Homo sapiens*. Humans have about 3 billion bases of information, divided into roughly 20,000 genes, which are spread among non-coding sequences and distributed among 24 distinct chromosomes (22 autosomes plus the X and Y sex chromosomes) (**Figure** 8.1). The **genome** is all of the hereditary information encoded in the DNA, including the genes and non-coding sequences. The Human Genome Project (See the *Biotechnology* chapter) has produced a reference sequence of the human genome. The human genome consists of protein-coding exons, associated introns and regulatory sequences, genes that encode other RNA molecules, and “junk” DNA, regions in which no function as yet been identified.

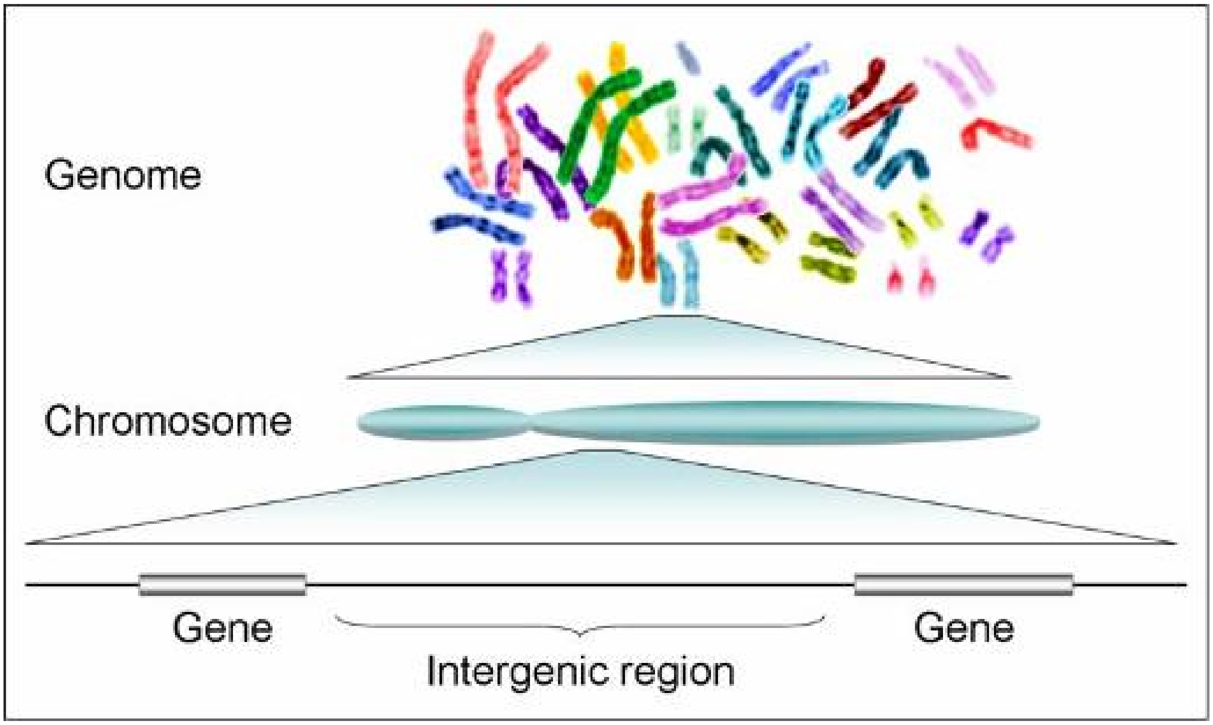


Figure 8.1: The Human Genome is depicted as the stained chromosomes at the top of the figure. The genome consists of chromosomes, which are composed of genes and other regions of DNA between the genes. Notice that there are 23 pairs of chromosomes.

Chromosomes and Genes

The human genome consists of 24 distinct chromosomes: 22 autosomal chromosomes plus the sex-determining X and Y chromosomes. A chromosome is a threadlike molecule of genes and other DNA located in the nucleus of a cell. Different organisms have different numbers of chromosomes. Human somatic cells have

23 chromosome pairs for a total of 46 chromosomes: two copies of the 22 autosomes (one from each parent), plus an X chromosome from the mother and either an X or Y chromosome from the father (**Figure** 8.2).

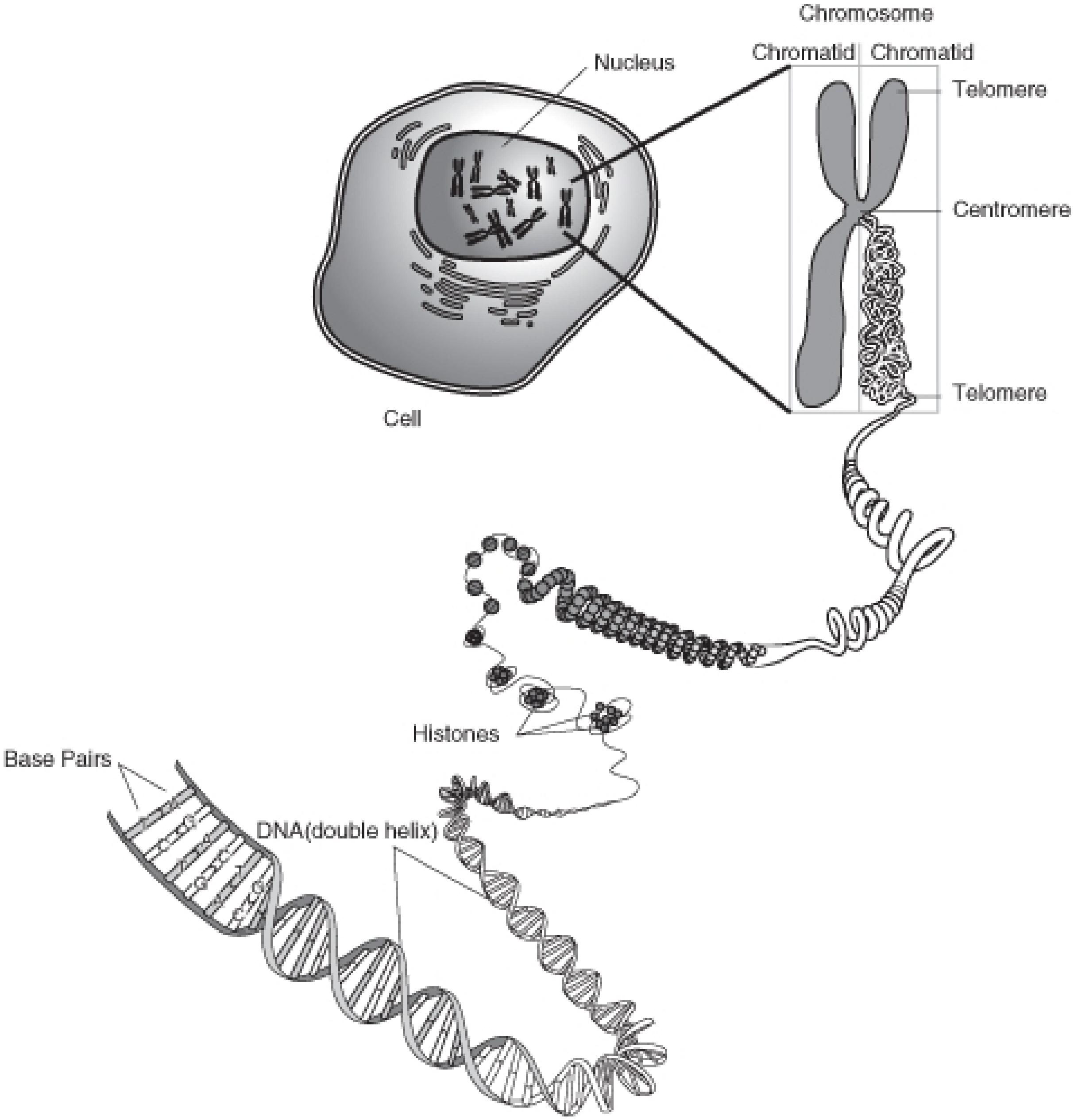


Figure 8.2: The human genome has 23 pairs of chromosomes located in the nucleus of somatic cells. Each chromosome is composed of genes and other DNA wound around histones (proteins) into a tightly coiled molecule.

There are an estimated 20,000 human protein-coding genes, but many more proteins. Most human genes have multiple exons separated by much larger introns. Regulatory sequences controlling gene expression are associated with exon sequences. The introns are usually excised (removed) during post-transcriptional modification of the mRNA. Human cells make significant use of alternative splicing (see the *Molecular Genetics* chapter) to produce a number of different proteins from a single gene. So even though the human genome is surprisingly similar in size to the genomes of simpler organisms, the human proteome is thought to be much larger. A **proteome** is the complete set of proteins expressed by a genome, cell, tissue, or organism.

Linkage

As stated above, our roughly 20,000 genes are located on 24 distinct chromosomes. **Linkage** refers to particular genetic loci, or alleles inherited together, suggesting that they are physically on the same chromosome, and located close together on that chromosome. Two or more loci that are on the same chromosome are physically connected and tend to segregate together during meiosis, unless a cross over event occurs between them. A crossing-over event during prophase I of meiosis is rare between loci that usually segregate together; these loci will usually be close together on the same chromosome. They are, therefore, said to be linked. Alleles for genes on different chromosomes are not linked; they sort independently (independent assortment) of each other during meiosis.

A gene is also said to be linked to a chromosome if it is physically located on that chromosome. For example, a gene (or loci) is said to be linked to the X-chromosome if it is physically located on the X-chromosome chromosome. The physical location of a gene is important when analyzing the inheritance patterns of phenotypes due to that gene. The inheritance patterns of phenotypes may be different if the gene is located on a sex chromosome or an autosome. This will be further discussed in the next lesson.

Linkage Maps

The frequency of recombination refers to the rate of crossing-over (recombination) events between two loci. This frequency can be used to estimate genetic distances between the two loci, and create a **linkage map**. In other words, the frequency can be used to estimate how close or how far apart the two loci are on the chromosome.

In the early 20th century, Thomas Hunt Morgan, working with the fruit fly *Drosophila Melanogaster*, demonstrated that the amount of crossing over between linked genes differs. This led to the idea that the frequency of crossover events would indicate the distance separating genes on a chromosome. Morgan's student, Alfred Sturtevant, developed the first genetic map, also called a linkage map.

Sturtevant proposed that the greater the distance between linked genes, the greater the chance that non-sister chromatids would cross over in the region between the genes during meiosis. By determining the number of recombinants - offspring in which a cross-over event has occured - it is possible to determine the approximate distance between the genes. This distance is called a genetic map unit (m.u.), or a **centimorgan**, and is defined as the distance between genes for which one product of meiosis in 100 products is a recombinant. So, a recombinant frequency of 1% (1 out of 100) is equivalent to 1 m.u. Loci with a recombinant frequency of 10% would be separated by 10 m.u. The recombination frequency will be 50% when two genes are widely separated on the same chromosome or are located on different chromosomes. This is the natural result of independent assortment. Linked genes have recombination frequencies less than 50%.

Determining recombination frequencies between genes located on the same chromosome allows a linkage map to be developed. Linkage mapping is critical for identifying the location of genes that cause genetic diseases.

Variation

As stated above, even though we essentially all have the same genes, the gene products work a little different in all of us, making us unique. That is, the variation within the human genome results in the uniqueness of our species. In fact, genetically speaking, we are all about 99.9% identical. However, it is this 0.1%

variation that results in our physical noticeable differences, as well as traumatic events such as illnesses or congenital deformities. These differences can also be used for societies benefits, such as through forensic DNA analysis (discussed in the *Biotechnology* chapter). Most studies of this genetic variation focus on small differences, know as **SNPs**, or **single nucleotide polymorphisms**, which are substitutions in individual bases along a chromosome. For example, the single base change from the sequence GGATAACGTCA to GGAAAACGTCA would be a SNP. Although not occurring uniformly, in the human genome, it has been estimated that SNPs occur every 1 in 100 to 1 in 1000 bases.

DNA sequences that repeat a number of times are known as **repetitive sequences** or repetitive elements. For example the sequence CACACACACACACA would be a dinucleotide (2 base) repeat, or the sequence GATCGATCGATCGATCGATC would be a tetranucleotide (4 base) repeat. The genomic loci and length of certain types of repetitive sequences are highly variable from person to person, which is the basis of DNA fingerprinting and DNA paternity testing technologies. Longer repetitive elements are also common in the human genome. Examples of repeat polymorphisms are described in **Table** 8.1

Table 8.1: **Repeat Polymorphisms (bp = base pair)**

Dinucleotide	repeats of two bp sequences
Tetranucleotide	repeats of four bp sequences
Microsatellite; Short Tandem Repeats (STRs)	short sequences of 100-200 bp, usually due to repeats of 1-6 bp sequences
Minisatellite	short sequences of 6-10 bp repeats
VNTR: Variable Number of Tandem Repeat	short nucleotide sequence ranging from 14 to 100 nucleotides long, organized into clusters of tandem repeats, usually repeated in the range of between 4 and 40 times per loci

Autosomes and Sex Chromosomes

There are 44 autosomes and 2 sex chromosomes in the human genome, for a total of 46 chromosomes (23 pairs). **Sex chromosomes** specify an organism's genetic sex. Humans can have two different sex chromosomes, one called X and the other Y. Normal females possess two X chromosomes and normal males one X and one Y. An **autosome** is any chromosome other than a sex chromosome. **Figure 3** 8.3 shows a representation of the 24 different human chromosomes. **Figure** 8.4 shows a karyotype of the human genome. A **karyotype** depicts, usually in a photograph, the chromosomal complement of an individual, including the number of chromosomes and any large chromosomal abnormalities. Karyotypes use chromosomes from the metaphase stage of mitosis.

The 22 autosomes are numbered based on size, with the largest chromosome labeled chromosome 1. These 22 chromosomes occur in homologous pairs in a normal diploid cell, with one of each pair inherited from each parent. The sex of an individual is determined by the sex chromosome within the male gamete. Females are homologous, XX, for the sex chromosomes, whereas males are heterozygous, XY. As all individuals inherit an X chromosome from their mother (females can only produce gametes with an X chromosome), it is the sex chromosome that they inherit from their father that determines their sex.

Both autosomal-linked and sex-linked traits and disorders will be discussed later in this chapter.

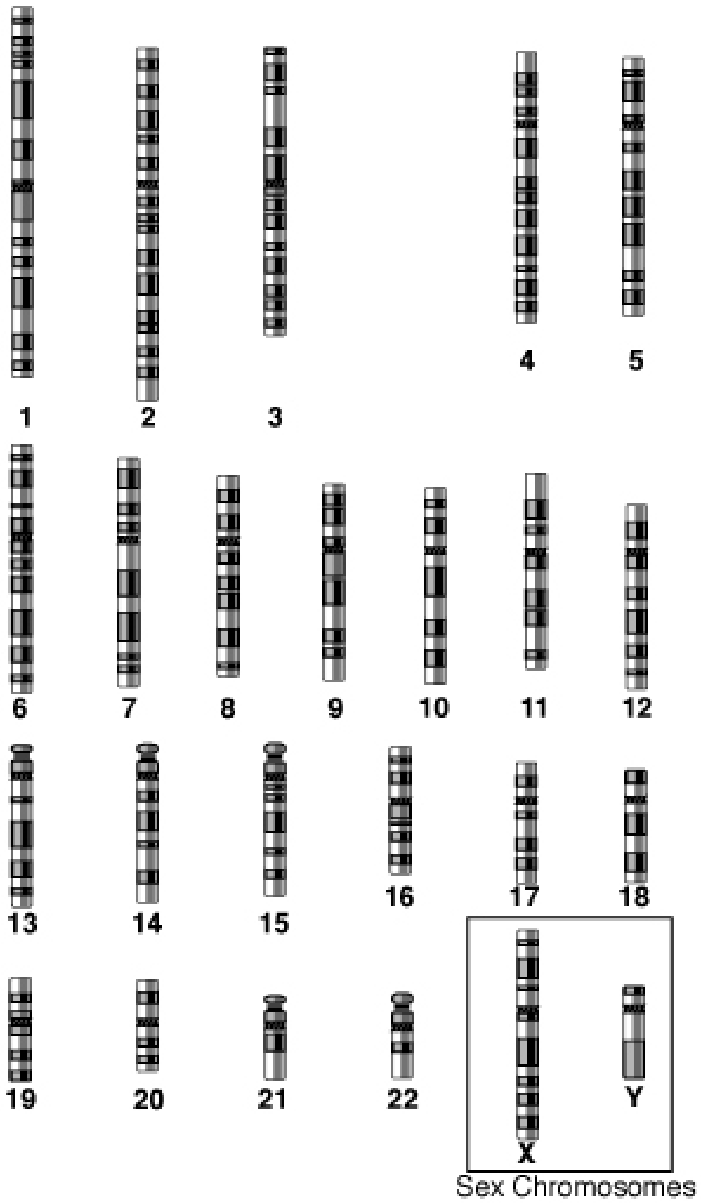


Figure 8.3: The 24 human chromosomes. The autosomes are numbered 1 - 22, based on size, with chromosome 1 being the largest. The X and Y sex chromosomes are shown in the box.

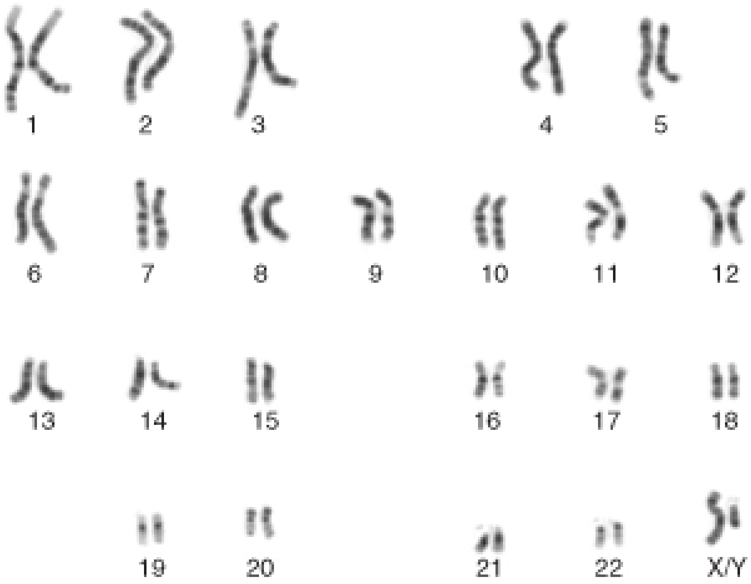


Figure 8.4: A karyotype of the human genome. Is this from a male or female?

Sex-Linked Genes

Sex-linked genes are located on either the X or Y chromosome, though it more commonly refers to genes located on the X-chromosome. For that reason, the genetics of **sex-linked** (or **X-linked**) diseases, disorders due to mutations in genes on the X-chromosome, results in a phenotype usually only seen in males. This will be discussed in the next lesson.

In humans, the Y chromosome spans 58 million bases and contains about 78 to 86 genes, which code for only 23 distinct proteins, making the Y chromosome one of the smallest chromosomes. The X chromosome, on the other hand, spans more than 153 million bases and represents about 5% of the total DNA in women's cells, 2.5% in men's cells. The X chromosome contains about 2,000 genes, however few, if any, have anything to do with sex determination. The Y chromosome is the sex-determining chromosome in humans and most other mammals. In mammals, it contains the gene **SRY** (sex-determining region Y), which encodes the testes-determining factor and triggers testis development, thus determining sex. It is the presence or absence of the Y chromosome that determines sex.

X-Inactivation

Early in embryonic development in females, one of the two X chromosomes is randomly inactivated in nearly all somatic cells. This process, called **X-inactivation**, ensures that females, like males, have only one functional copy of the X chromosome in each cell. X-inactivation creates a Barr body, named after their discover, Murray Barr. The Barr body chromosome is generally considered to be inactive, however there are a small number of genes that remain active and are expressed.

Lesson Summary

- A genetic disease is a phenotype due to a mutation in a gene or chromosome.
- Many of these mutations are present at conception, and are therefore in every cell of the body.
- Mutant alleles may be inherited from one of both parents, resulting in a dominant or recessive hereditary disease.

- Currently there are over 4,000 known genetic disorders, with many more phenotypes yet identified.
- The genome refers to all the DNA of a particular species.
- The human genome consists of 24 distinct chromosomes: 22 autosomal chromosomes, plus the sex-determining X and Y chromosomes.
- Linkage refers to particular genetic loci or alleles inherited together, suggesting that they are physically on the same chromosome, and located close together on that chromosome.
- The variation within the human genome results in the uniqueness of our species.
- There are 44 autosomes and 2 sex chromosomes in the human genome, for a total of 46 chromosomes.
- Sex chromosomes specify an organism's genetic sex. Humans have two different sex chromosomes, one called X and the other Y.
- Sex-linked genes are located on either the X or Y chromosome, though it more commonly refers to genes located on the X-chromosome.
- Early in embryonic development in females, one of the two X chromosomes is randomly inactivated in nearly all somatic cells. This process is called X-inactivation.

Review Questions

1. What is a genetic disease?
2. Discuss the main difference between autosomal and sex-linked.
3. Why is variation within the human genome important?
4. Why is it more common for males to have X-linked disorders?
5. Describe how a mutation can lead to a genetic disease.
6. Discuss how a new mutation can become a new dominant allele.
7. How are autosomal traits usually inherited? Give examples of traits.
8. How are genetic diseases usually inherited? Are there exceptions? Research examples.

Further Reading / Supplemental Links

- The National Human Genome research Institute:
- http://www.genome.gov
- The Dolan DNA Learning Center:
- http://www.dnalc.org/home_alternate.html
- DNA Interactive:
- http://www.dnai.org/
- A Science Odyssey: DNA Workshop:
- http://www.pbs.org/wgbh/aso/tryit/dna/
- Kimball's Biology Pages:
- http://users.rcn.com/jkimball.ma.ultranet/BiologyPages
- http://en.wikipedia.org

Vocabulary

autosome Any chromosome other than a sex chromosome.

Barr body The inactive X-chromosome in females.

chromosome A threadlike molecule of genes and other DNA wound around histone proteins; located in the nucleus of a cell.

genetic counselor An individual trained in human genetics and counseling.

genetic disease A phenotype due to a mutation in a gene or chromosome.

geneticist A medical doctor specializing in genetic disorders.

genetics The branch of biology that focuses on heredity.

genome All of the hereditary information encoded in the DNA, including the genes and non-coding sequences.

karyotype Depicts, usually in a photograph, the chromosomal complement of an individual, including the number of chromosomes and any large chromosomal abnormalities.

linkage Refers to particular genetic loci or alleles inherited together, suggesting that they are physically on the same chromosome, and located close together on that chromosome.

microsatellite Short sequences of 100-200 bp, usually due to repeats of 1-6 bp sequences; also known as a STR (Short Tandem Repeat) polymorphism.

minisatellite Short sequence polymorphisms of 6-10 bp repeats.

proteome The complete set of proteins expressed by a genome, cell, tissue, or organism.

repetitive sequences DNA sequences that repeat a number of times; also known as repetitive elements.

sex chromosomes Specify an organism's genetic sex; in humans, the X and Y chromosomes.

sex-linked disease A disorder due to a mutation in a gene on the X-chromosome; also called X-linked disorder.

SNPs Single Nucleotide Polymorphisms; substitutions in individual bases along a gene or chromosome.

SRY Sex-determining region Y; gene which encodes the testes-determining factor and triggers testis development, thus determining sex; located on the Y chromosome.

VNTR Variable Number of Tandem Repeat; short nucleotide sequence ranging from 14 to 100 nucleotides long, organized into clusters of tandem repeats, usually repeated in the range between 4 and 40 times per loci.

X-inactivation The random inactivation of one X-chromosome in females; occurs early in embryonic development.

Points to Consider

- How are traits inherited? How about the inheritance of genetic disorders? Are inheritance patterns of traits and disorders similar?
- Could simple Mendelian inheritance account for such complex traits with vast phenotypic variation such as height or skin color? What do you think?

8.2 Human Inheritance

Lesson Objectives

- Describe the difference between a genetic trait and a genetic disease/disorder.
- Define the various modes of inheritance, focusing on the differences between autosomal and sex-linked.
- Gives examples of dominant and recessive genetic disorders.
- Discuss the inheritance of sex-linked traits.
- Discuss complex inheritance patterns.
- Define codominant alleles and give examples.
- Define incomplete dominance.
- Give examples of multiple allele traits.
- Discuss how a trisomy condition may be detected.
- What is Down syndrome?
- List some examples of phenotypes due to abnormal numbers of sex chromosomes.
- Discuss the importance of gene therapy.
- Describe the most common method of gene therapy.

Introduction

What is a genetic trait? Is a genetic disease a trait? The answer to these questions may be debated, but a genetic trait is a characteristic of you encoded in your DNA. Could you say that a genetic disease is encoded in your DNA? Well, by definition, yes you can.

How are traits inherited? Do different traits have different patterns of inheritance? Is it as simple as a one allele – one phenotype relationship? Or is it more complex? Is there a difference if the gene is located on an autosome or a sex chromosome? Can there be traits due to multiple genes? The answer to all of the above questions is a resounding 'sometimes.' Sometimes it is as simple as a one allele – one phenotype relationship, sometimes it is more complex. Sometimes there is a difference depending on the location of the gene. Sometimes traits can be due to multiple genes. Human genetics is an exciting aspect of biology and medicine; an aspect of biology that is extremely important to our health and well being.

Autosomal and Sex-Linked Traits: Mutations and Genetic Disorders

Autosomal vs. sex-linked. In terms of genetics, is the location of a gene or trait an important piece of information? Does it make a difference if the gene is located on a sex chromosome or an autosome? It might. Remember from lesson 9.1 that sex chromosomes determine an organism's sex, so the autosomes are the other chromosomes. Autosomal-linked traits are due to genes on the **autosomes**; **sex-linked traits** are due to genes located on the **sex chromosomes**.

What is the difference between a trait and a genetic disorder? Could a disorder be considered a trait? We tend to think of traits as hair color or skin color and disorders as something that is bad for you. But in terms of genetics, a genetic disorder is a trait. Both may be due to your genes.

Simple Dominant Heredity

How are traits due to genes on autosomes inherited? Autosomal traits due to the effects of one gene are usually inherited in a simple Mendelian pattern. That is, they can be either dominant or recessive. In humans, whereas many genetic disorders are inherited in a recessive manner, simple dominant inheritance accounts for many of a person's physical characteristics, such as chin, earlobe, hairline and thumb shape. For example, having earlobes that are attached to the head is a recessive trait, whereas heterozygous and homozygous dominant individuals have freely hanging earlobes. If you have a cleft chin, a pointed frontal hairline (called a widow's peak), or a hitchhiker's thumb, you have inherited the dominant allele for each characteristic from at least one of your parents. Other dominant traits include the presence of hair on the middle section of your fingers, thick lips, and almond-shaped eyes. A widow's peak and earlobe shape are displayed in **Figure** 8.5 and **Figure** 8.6.

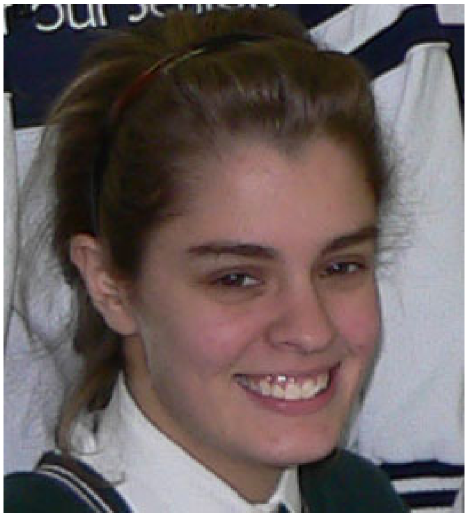


Figure 8.5: A young woman with a widow

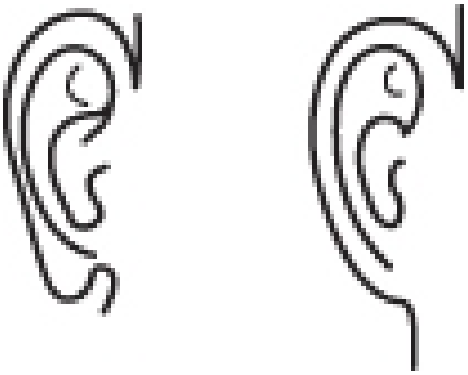


Figure 8.6: A diagram showing free (left) and attached (right) earlobes. Attached earlobes is a recessive trait.

Mutations and Genetic Disorders

Mutations, changes in the DNA or RNA sequence, can have significant phenotypic effects or no effects. We have previously discussed various types of mutations. Now, let's discuss the outcomes of some of those mutations. As mentioned at the beginning of this chapter, a genetic disorder is a condition caused by abnormalities, such as mutations, in your genes or chromosomes. Genetic disorders are usually present from conception. These disorders include chromosomal abnormalities, in which the individual has too few or too many chromosomes or chromosomes with large alterations, or diseases due to a mutation in a specific gene. These defective genes are usually inherited from the parents, hence the term hereditary disease or genetic disorder. Genetic disorders can be inherited in a dominant or recessive manner (**Figure** 8.7 and **Figure** 8.8). Recessive disorders require the inheritance of a defective gene from each parent. The parents are usually unaffected and are healthy carriers of the defective gene.

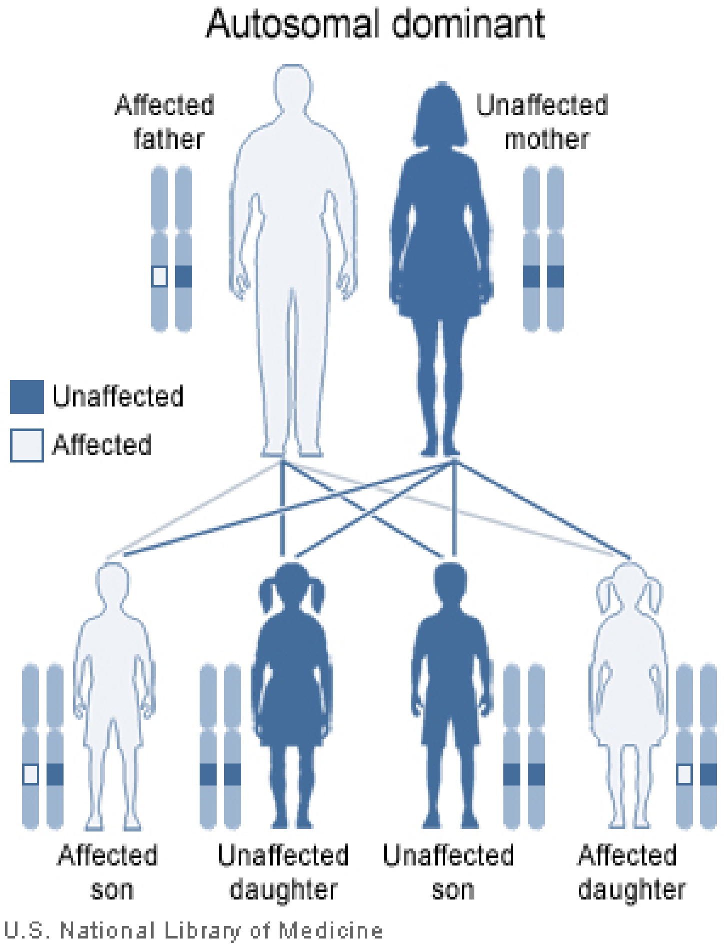


Figure 8.7: Autosomal Dominant Inheritance. Only one

How can you, or a geneticist, determine the inheritance pattern of a phenotype? A **pedigree**, which is essentially a representation of genetic inheritance, is helpful. A pedigree is a chart, much like a family tree, which shows all of the known individuals within a family with a particular phenotype (**Table** 8.2). Pedigrees have been discussed in the chapter titled *Mendelian Genetics.* Examples of autosomally inherited disorders include cystic fibrosis, Tay-Sachs disease, phenylketonuria, and achondroplasia.

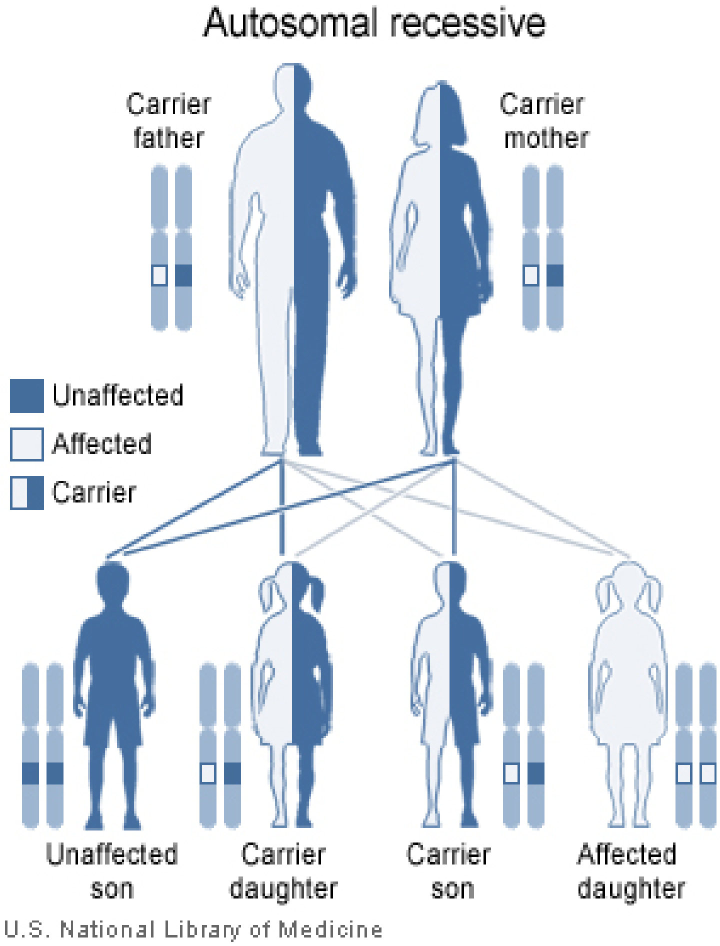


Figure 8.8: Autosomal Recessive inheritance. For a genetic disease inherited in this manner, two mutant alleles are necessary to result in the phenotype. Tay-Sachs Disease (discussed later) is an example of a recessive disorder. Notice that both parents are unaffected carriers of the mutant allele. These unaffected carriers allow the allele to be maintained in the gene pool - the complete set of a population's genes. Even if the allele is lethal in the homozygous recessive condition, the allele will be maintained through heterozygous individuals.

Table 8.2: **Autosomal and Sex-linked Inheritance Patterns**

Inheritance Pattern	Description	Example
Autosomal Dominant	Only one mutated allele is needed for a person to be affected by an **autosomal dominant disorder**. Each affected person usualy has one affected parent. There is a 50% chance that a child will inherit the mutated gene.	Huntingtons disease, Achondroplasia, Neurofibromatosis 1, Marfan Syndrome, Hereditary nonpolyposis colorectal cancer
Autosomal Recessive	Both copies of the gene must be mutated for a person to be affected by an **autosomal recessive disorder**. An affected person usually has unaffected parents who each carry a single copy of the mutated gene (and are referred to as carriers).	Cystic fibrosis, Sickle cell anemia, Tay-Sachs disease, Spinal muscular atrophy
X-linked Dominant	**X-linked dominant disorders** are caused by mutations in genes on the X chromosome. Only a few disorders have this inheritance pattern.	
X-linked Recessive	**X-linked recessive disorders** are also caused by mutations in genes on the X chromosome. Males are more frequently affected than females. The sons of a man with an X-linked recessive disorder will not be affected, and his daughters will carry one copy of the mutated gene. A woman who carries an X-linked recessive disorder has a 50% chance of having sons who are affected and a 50% chance of having daughters who carry one copy of the mutated gene.	Hemophilia A, Duchenne muscular dystrophy, Color blindness
Y-Linked	**Y-linked disorders** are caused by mutations on the Y chromosome. Only males can get them, and all of the sons of an affected father are affected. Y-linked disorders only cause infertility, and may be circumvented with the help of some fertility treatments.	Male Infertility

Cystic Fibrosis

Cystic fibrosis (CF) is a recessive inheritable disorder caused by a mutation in a gene called the cystic fibrosis transmembrane conductance regulator (CFTR). The product of this gene is a chloride ion channel important in creating sweat, digestive juices, and mucus. Although most people without CF have two working copies of the CFTR gene, only one is needed to prevent cystic fibrosis. CF develops when individuals have a mutation in both copies of the gene, such that neither gene product works normally. CF is one of the most common life shortening diseases. Diagnosis is usually made in childhood. In the United States, approximately 1 in 3,900 children is born with CF (**Figure** 8.9). One in 22 people of European descent are carriers of a mutated CFTR gene. CF mainly affects the lungs and digestive system, causing difficulty breathing due to thick mucus production, progressive disability, and for some individuals, premature death.

Individuals can be diagnosed prior to birth by genetic testing. Because development of CF in the fetus requires each parent to pass on a mutated copy of the CFTR gene and because CF testing is expensive, testing is often initially performed on just one parent. If that parent is found to be a carrier of a CFTR gene mutation, the other parent is then tested to calculate the risk that their children will have CF. CF can result from more than a thousand different mutations; currently it is not possible to test for each one. As new DNA testing methodologies are developed, testing for more mutations will become more common and less expensive. Testing analyzes DNA for the most common mutations, such as a deletion of amino acid 508 (phenylalenine, also known as ΔF508). If a family has a known uncommon mutation, specific screening for that mutation can be performed. However, it must be noted that because there may be other not yet identified mutations that result in CF, and as not all known mutations are found on current tests, a negative screen does not guarantee that a child will not have CF.

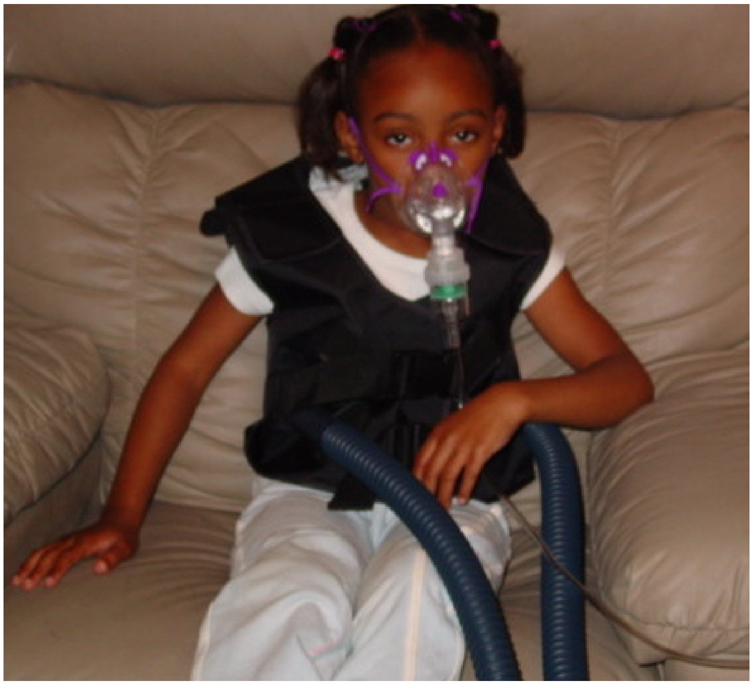


Figure 8.9: A young cystic fibrosis patient undergoing breathing treatment. Cystic fibrosis is a recessively inherited genetic disorder.

Tay-Scahs Disease

Tay-Sachs disease is a genetic disorder that is fatal in its most common variant, known as Infantile Tay-Sachs disease. Tay-Sachs is an autosomal recessive disorder, requiring the inheritance of a defective gene from each parent. The disease results from the accumulation of harmful quantities of fat in the nerve cells of the brain. Tay-Sachs results from mutations in the HEXA gene located on chromosome 15, which encodes the alpha-subunit of the lysosomal enzyme beta-N-acetylhexosaminidase A, which normally breaks down the fat. More than 90 mutations, including substitutions, insertions, deletions, splice site mutations, and other more complex patterns have been characterized in this gene, and new mutations are still being reported. Each of these mutations alters the protein product, inhibiting the function of the enzyme.

Tay-Sachs disease is a rare disease. Unaffected carriers of a Tay-Sachs allele may not know they have the allele. Other autosomal disorders such as cystic fibrosis and sickle cell anemia are far more common. The importance of Tay-Sachs lies in the fact that an inexpensive enzyme assay test was developed. The automation of this analysis has provided one of the first ”mass screening” tools in medical genetics. Two unaffected carriers can have a child homozygous for a Tay-Sachs allele, resulting, currently, in a lethal phenotype. Tay-Sachs alleles are maintained in a population through these unknowing heterozygous carriers.

The analysis and screening for Tay-Sachs has became a research and public health model for understanding and preventing all autosomal genetic disorders. Another genetic disease that is easily analyzed in phenylketonuria.

Phenylketonuria

Phenylketonuria (PKU) is an autosomal recessive genetic disorder characterized the inability to metabolize the amino acid phenylalanine. PKU is due to a deficiency in the enzyme phenylalanine hydroxylase (PAH). When PAH is deficient, phenylalanine accumulates and is converted into phenylketones, which can be detected in the urine. Left untreated, this condition can cause problems with brain development, leading to progressive mental retardation and seizures. However, PKU can be treated with a specific diet, one low in phenylalanine. A diet low in phenylalanine and high in tyrosine can bring about a nearly total cure.

The incidence of PKU is about 1 in 15,000 live births. In the United States PKU is screened at birth as part of a national biochemical screening program, for every baby born in a hospital. Babies born at home may not be screened. If PKU is diagnosed early enough, an affected newborn can grow up with normal brain development, but only by eating a special diet low in phenylalanine for the rest of his or her life. In essence, this is a protein-free diet. This requires severely restricting or eliminating foods high in protein content (containing phenylalanine), such as breast milk, meat, chicken, fish, nuts, cheese and other dairy products. Starchy foods such as potatoes, bread, pasta, and corn must also be monitored. Many diet foods and diet soft drinks that contain the sweetener aspartame must also be avoided, as aspartame consists of two amino acids: phenylalanine and aspartic acid. Supplementary infant formulas are used in these patients to provide the amino acids and other necessary nutrients that would otherwise be lacking in their diet. Since phenylalanine is required for the synthesis of many proteins, it is necessary to have some of this amino acid, but levels must be strictly controlled. In addition, tyrosine, which is normally derived from phenylalanine, must also be supplemented.

Achondroplasia

Whereas cystic fibrosis, Tay-Sachs, and phenylketonuria are all autosomal recessive disorders, **achondroplasia** is an autosomal dominant disorder. Achondroplasia is the most common cause of dwarfism. Achondroplasia is a result of an autosomal dominant mutation in the fibroblast growth factor receptor gene

3 (FGFR3), which causes an abnormality of cartilage formation. FGFR3 normally has a negative regulatory effect on bone growth. In achondroplasia, the mutated form of the receptor is constitutively active (constantly "turned on") and this leads to severely shortened bones. Individuals with achondroplasia are heterozygous for the mutation (one mutant copy, one normal copy). Homozygous for the achondroplasia mutation is lethal prior to birth or shortly after birth.

For autosomal dominant disorders, a person with the disorder has a 50% chance of passing on the gene to their offspring. For achondroplasia, this means there will be a 50% chance that each child will have achondroplasia. Since two copies are fatal, if two people with achondroplasia have a child, there is a 25% chance of the child dying shortly after birth, a 50% chance the child will have achondroplasia, and a 25% chance the child will have a normal phenotype. However, in 3 out of 4 cases, people with achondroplasia are born to parents who don't have the condition. This is the result of a new mutation. New achondroplasis mutations are associated with increasing paternal age (over 35 years). Studies have demonstrated that new gene mutations are exclusively inherited from the father and occur during spermatogenesis. More than 98% of achondroplasia is caused by a G to A point mutation at nucleotide 1138 of the FGFR3 gene, which causes a glycine to arginine substitution. This makes this particular nucleotide one of the most, if not the most, mutable base in the human genome.

There are three other syndromes with a genetic basis similar to achondroplasia: hypochondroplasia, thanatophoric dysplasia, and SADDAN Dysplasia (severe achondroplasia, developmental delay, acanthosis nigricans (a skin condition)). Each of these disorders is also caused by a mutation in the *FGFR3* gene. Each of the conditions results in a distinct difference in the degree of severity of the phenotype, with hypochondroplasia having the mildest phenotype. Other genes in which mutations cause a phenotypic spectrum of disease include the collagen genes among others.

Sex-Linked Traits

Traits controlled by genes located on the sex chromosomes (X and Y) are called sex-linked traits (**Figure** 8.10). Remember, females have two X chromosomes and males have a X and a Y chromosome. Therefore, any recessive allele on the X chromosome of a male will not be masked by a dominant allele. X-linked traits include the hemophilia and color blindness. Hemophilia is the name of a family of hereditary genetic illnesses that impair the body's ability to control coagulation. Color Blindness, or color vision deficiency, in humans is the inability to perceive differences between some or all colors that other people can distinguish.

Hemophilia is a group of diseases in which blood does not clot normally. Factors in blood are involved in clotting. Hemophiliacs lacking the normal Factor VIII are said to have Hemophilia A, the most common form. England's Queen Victoria was a carrier for this disease. The allele was passed to two of her daughters and one son. Since royal families in Europe commonly intermarried, the allele spread, and may have contributed to the downfall of the Russian monarchy.

Genetic red-green color blindness affects men much more often than women, because the genes for the red and green color receptors are located on the X chromosome. Females are red-green color blind only if both of their X chromosomes carry the defective gene, whereas males are color blind if their single X chromosome carries the defective gene. As males have only the one X-chromosome, the gene for red-green color blindness is transmitted from a color blind male to all his daughters, who are usually heterozygous carriers and therefore unaffected. Subsequently, this carrier woman has a fifty percent chance of passing on a X chromosome with a defective gene to each of her male offspring. The sons of an affected male will not inherit the trait from him, since they receive his Y chromosome and not his X chromosome. Should an affected male have children with a carrier or colorblind woman, their daughters may be colorblind by inheriting a X chromosome with the mutant gene from each parent.

Muscular dystrophy is a term encompassing a variety of muscle wasting diseases. The most common

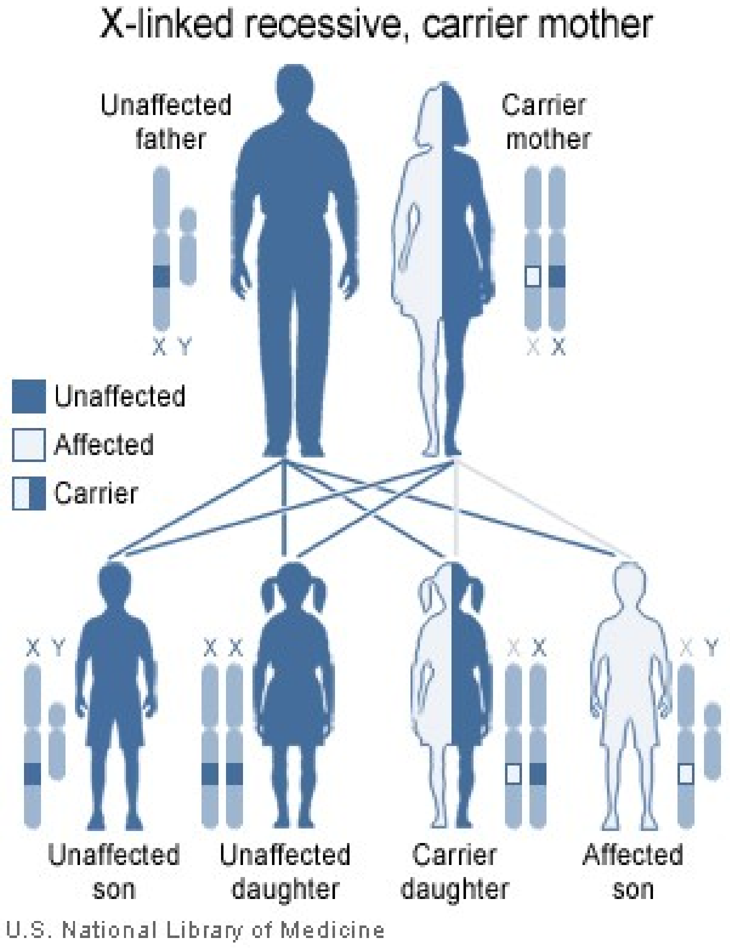


Figure 8.10: X-linked recessive inheritance. As boys have only one X-chromosome, if they inherit the mutant allele from their mother, they will possess the phenotype that results from that allele.

type, **Duchenne Muscular Dystrophy** (DMD), affects cardiac and skeletal muscle, as well as some mental functions. DMD is an X-linked recessive disorder occurring in 1 in 3,500 newborns. Most affected individuals die before their 20th birthday.

Complex Traits

So far we have discussed traits inherited in a simple Mendelian pattern. Either the trait is dominate or recessive. The trait is affected by only one gene. But this is not the case for many genes; rarely is inheritance that simple. More complex patterns of inheritance are common. These were introduced in the chapter titled *Mendelian Genetics.*

Mendel's pea plants showed complete dominance of one allele over the other. The offspring always completely looked like one of the parents – there was never any phenotype ‘‘in between" the two parents. The heterozygous individuals were indistinguishable from the homozygous dominant individuals. Is it possible for both alleles to be dominant, or neither to be completely dominant? The answer to both of these questions is yes.

Codominance

Codominance is when two alleles are both expressed in the heterozygous individual; that is, they both affect the phenotype in separate and distinguishable ways (**Figure** 8.11). The A, B alleles of the ABO blood group system are a classic example, and these have been discussed in the chapter titled *Mendelian Genetics.* The A and B alleles are codominant with each other. When a person has both an A and a B allele, the person has type AB blood. When two persons with AB blood type have children, the children can be type A, type B, or type AB. There is a 1A:2AB:1B phenotype ratio instead of the 3:1 phenotype ratio found when one allele is dominant and the other is recessive.

Incomplete Dominance

Incomplete dominance is seen in heterozygous individuals with an intermediate phenotype. For example, if Mendel had ever observed a medium stem length plant when a tall and short plant were crossed, that would have suggested incomplete dominance. In incomplete dominant situations, the phenotype expression is dependent on the dosage of the genes. Two copies of the gene result in full expression, while only one copy produces partial expression and an intermediate phenotype.

Multiple-Allele Traits

Traits controlled by more than two alleles have multiple alleles. Theoretically, any base change will result in a new allele. In fact, within the human population, it may be safe to say that most human genes have more than 2 alleles. Whereas, we think of base changes, or mutations, as resulting in a new phenotype or disease, many base changes result in alleles that do not cause significant change in phenotypes. This is common in collagen genes, for example. The best characterized example of multiple alleles in humans is the ABO blood groups, discussed in the chapter titled *Mendelian Genetics.*

It is easiest to consider situations where each gene affects only one phenotypic characteristic. However, other situations where genes have other effects are common. As mentioned above, multiple alleles resulting in multiple phenotypes are not uncommon.

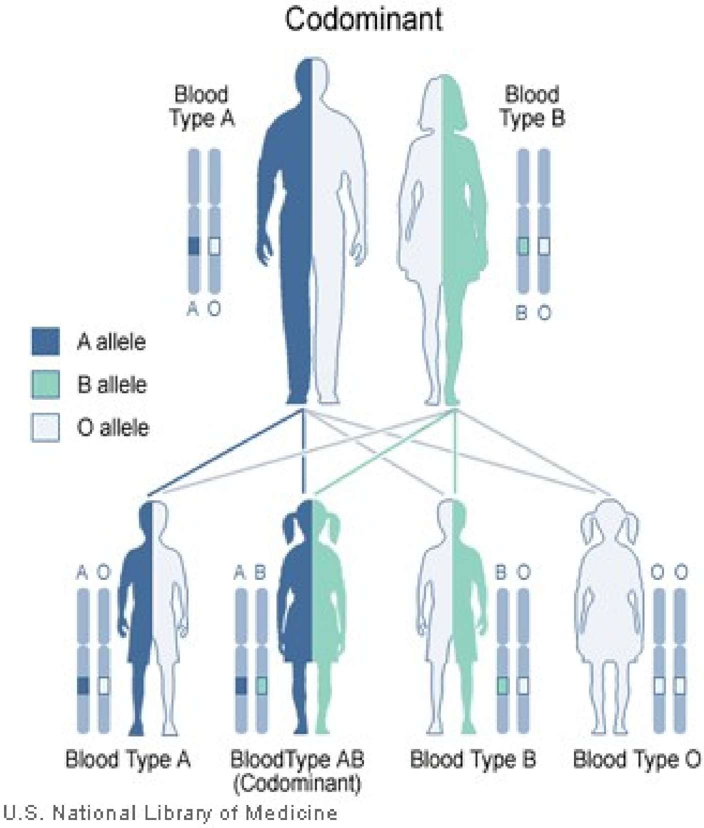


Figure 8.11: Codominant Inheritance. The A and B alleles are codominant. An AB heterozygous individual has type AB blood.

Pleiotropy

Many genes have multiple phenotypic effects, a property called **pleiotropy**. Thus, a new mutation in the gene will affect all the phenotypes/traits associated with the gene simultaneously. For example, the symptoms associated with sickle-cell disease are due to pleiotropic alleles. Another example is the collagen genes mentioned above. As you will learn later, many bones develop from a cartilage template. This cartilage template is made out of many proteins, with type II collagen, the predominant protein in the cartilage. The gene for this collagen, COL2A1, when mutated, not only affects the skeletal system, but due to its pleiotropic nature, it may also affect a person's eyes and hearing.

Epistasis

Epistasis is when a gene at one location (locus) alters the phenotypic expression of a gene at another locus. This is seen in the inheritance of coat color in mice. Epistasis takes place when the action of one gene is modified by one or several other genes, which are sometimes called modifier genes. The gene whose phenotype is expressed is said to be epistatic, while the phenotype altered or suppressed is said to be hypostatic.

Polygenic Traits

Polygenic traits are due to the actions of more than one gene and often, their interaction with the environment. These usually result in a measurable range in phenotype, such as height, eye color or skin color. These are known as multifactoral or quantitative characteristics. Polygenic inheritance results in an additive effect of the genes on a single phenotype.

Skin color is a polygenic trait and obviously demonstrates quantitative characteristics. A number of genes factor into determining a person's natural skin color, so modifying only one of those genes changes the color only slightly. It is currently thought that at least three separately inherited genes contribute to skin pigmentation. Let's call these three genes A, B, and C. A, B, and C are incompletely dominant to a, b, and c, with A, B, and C each contributing a "unit of darkness" to the phenotype. Therefore an AABBCC individual is very dark, darker than an AaBbCc individual, and much darker than a aabbcc individual. A person may have as many as 6 "dark units" to as few as no "dark units," and any combination in between. This will result in a phenotypic spectrum of color gradation.

Many disorders with genetic components are polygenic, including autism, certain cancers, diabetes and numerous others. Most phenotypic characteristics are the result of the interaction of multiple genes. The environment plays a significant role in many of these phenotypes. But what happens when multiple genes are either missing or duplicated?

Changes in Chromosome Number

So far we have focused on traits due to one gene or several genes. But what about many genes? What would happen if an entire chromosome were missing or duplicated? What if a human had only 45 chromosomes? Or 47? This real possibility is usually due to mistakes during meiosis; the chromosomes do not fully separate from each other during sperm or egg formation. Specifically, **nondisjunction** is the failure of replicated chromosomes to separate during anaphase II. If a zygote forms from a gamete lacking a chromosome, a viable embryo cannot be produced. Most human abnormal chromosome numbers result in the death of the developing embryo, often before a woman even realizes she is pregnant. Occasionally, a zygote with an extra chromosome can become a viable embryo and develop.

Trisomy is a state where humans have an extra autosome. That is, they have three of a particular chromosome instead of two. For example, trisomy 18 results from an extra chromosome 18, resulting in 47 total chromosomes. To identify the chromosome number (including an abnormal number), a sample of cells is removed from an individual or developing fetus. Metaphase chromosomes are photographed and a karyotype is produced. A karyotype will display any abnormalities in chromosome number or large chromosomal rearrangements. Trisomy 8, 9, 12, 13, 16, 18, and 21 have been identified in humans. Trisomy 16 is the most common trisomy in humans, occurring in more than 1% of pregnancies. This condition, however, usually results in spontaneous miscarriage in the first trimester. The most common trisomy in viable births is **Trisomy 21**.

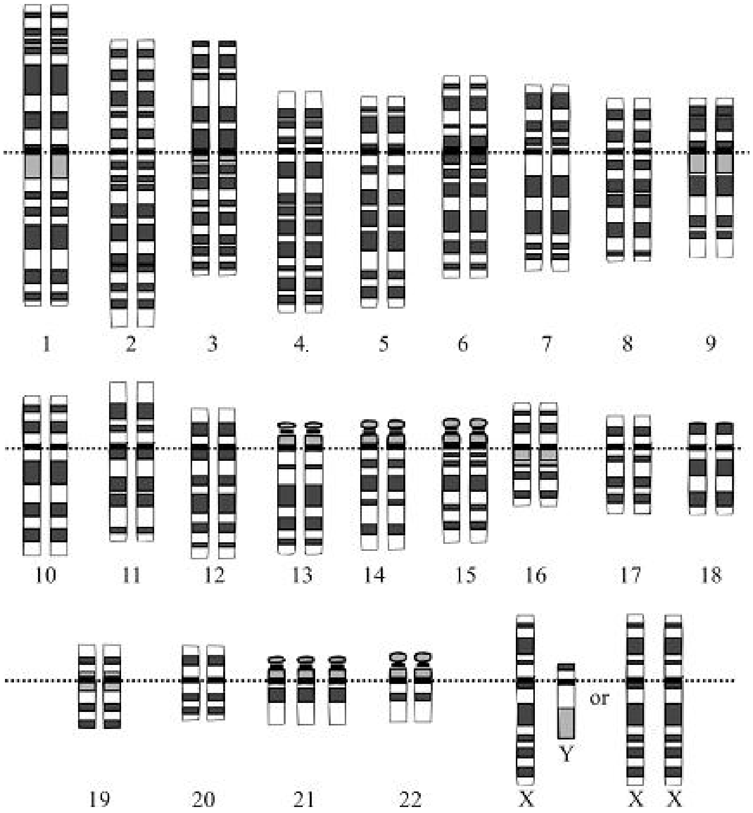


Figure 8.12: Trisomy 21 (Down Syndrome) Karyotype. Note the extra chromosome 21.

Trisomy 21: Down Syndrome

One of the most common chromosome abnormalities is Down syndrome, due to nondisjunction of chromosome 21 resulting in an extra complete chromosome 21, or part of chromosome 21 (**Figure** 8.13). Down syndrome is the only autosomal trisomy where an affected individual may survive to adulthood. Individuals with Down syndrome often have some degree of mental retardation, some impairment of physical growth, and a specific facial appearance. With proper assistance, individuals with Down syndrome can become successful, contributing members of society (**Figure** 8.14). The incidence of Down syndrome increases with maternal age.

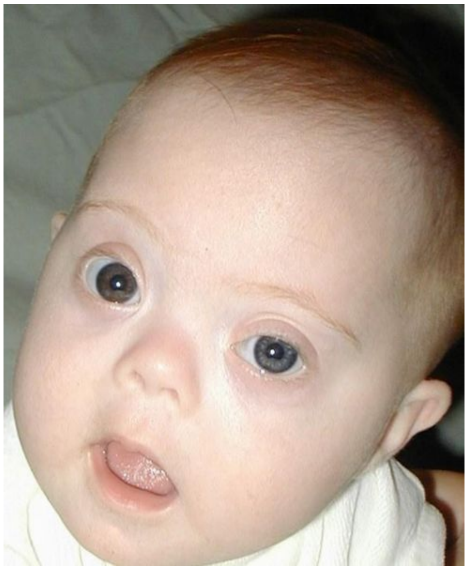


Figure 8.13: Child with Down syndrome, exhibiting characteristic facial appearance.

Figure 8.14: Boy with Down Syndrome assembling a bookcase.

Abnormal Numbers of Sex Chromosomes

What about when a person has more than 2 Y chromosomes, or more than 2 X chromosomes? Or a female with only one X chromosome? Sex-chromosome abnormalities may be caused by nondisjunction of one or more sex chromosomes. Many conditions are known in which there are an abnormal number of sex chromosomes. An X chromosome may be missing (XO), or there may be an extra one (XXX or XXY). There may also be an extra Y chromosome (XYY). Any combination of X and Y chromosomes, as long as there is a Y chromosome, will produce a male (up to XXXXY). These individuals can lead relatively normal lives, but they cannot have children. They may also have some degree of mental retardation. These syndromes include Klinefelter's syndrome, Turner syndrome and trisomy X.

Klinefelter's syndrome is caused by the presence of one or more extra copies of the X chromosome in a male's cells. Extra genetic material from the X chromosome interferes with male sexual development, preventing the testicles from functioning normally and reducing the levels of testosterone. Triple X syndrome (**trisomy X**) results from an extra copy of the X chromosome in each of a female's cells. Females with trisomy X have a lower IQ than their siblings. Turner syndrome results when each of a female's cells has one normal X chromosome and the other sex chromosome is missing or altered. The missing genetic material affects development and causes the characteristic features of the condition, including short stature and infertility.

Diagnosis and Treatment of Genetic Disorders

If someone has a rare genetic disease in her family, can she still have a baby? Is she predisposed to pass that phenotype along to her child? These are questions for a professional trained in human genetics. A geneticist and **genetic counselor** are usually involved in the diagnosis and treatment of human genetic disorders. Families with a genetic disease are referred to a genetic counselor, especially when they wish to determine a baby's likelihood of inheriting a genetic disease.

Individuals or their families at risk of inheriting a genetic disorder have many questions. What exactly is a genetic disorder? How does a person get it? Can it be passed onto the next generation? Can it be treated? What are the symptoms? Do the symptoms get worse with age? These and many more questions are where a genetic specialist, such as a genetic counselor can help. **Genetic counseling** is the process by which individuals or their families who are at risk of an inherited disorder, are counseled on many different aspects of the disorder. Genetic counseling may be necessary at any time throughout life, from before pregnancy to adulthood. Before pregnancy, genetic counseling would be appropriate for at risk individuals who are planning a family, such as when one or both individuals are either carriers or have a certain genetic trait. During pregnancy, genetic counseling is necessary for couples if the woman will be over 35 years of age at the time of delivery, if prenatal testing is recommended for any reason, or if an abnormality is noted on an ultrasound or other test. After birth, genetic counseling is appropriate if a birth defect is detected. During childhood, genetic counseling is appropriate if the child manifests any signs of developmental delay or a genetic syndrome, and in adulthood, genetic counseling is appropriate if signs of an adult onset genetic disorder is detected. During genetic counseling, individuals are advised of the consequences and nature of the disorder, the probability of developing or transmitting the disorder, and the options open to them in management and family planning in order to make appropriate decisions. In terms of the actual diagnosis of the disease, molecular analysis may be necessary; this will be discussed in the chapter titled Biotechnology.

Prenatal Diagnosis

”Is it possible to test the developing baby for potential genetic problems? Do you need to remove some of the baby’s DNA? How do you do that?” These questions are appropriate for a geneticist. Sometimes, to make sure the baby is developing properly, prenatal diagnosis is necessary. **Prenatal diagnosis** refers to the diagnosis of a disease or condition before the baby is born. The reason for prenatal diagnosis is to detect birth defects such as neural tube defects, chromosome abnormalities, genetic diseases and other conditions. It can also be used to determine the sex of the unborn baby, though this can usually be determined by an ultrasonography (ultrasound).

Diagnostic prenatal testing can be by invasive methods or non-invasive methods. Non-invasive methods are much less risky to the patient. Non-invasive methods can only evaluate the risk of a condition and cannot actually determine if the fetus has a condition. Non-invasive techniques include examinations of the mother’s womb through ultrasonography and analysis of maternal serum. If an abnormality is indicated by a non-invasive procedure, a more invasive technique may be employed to gather more information. **Amniocentesis** and **chorionic villus sampling** (CVS) are invasive procedures. These involve probes or needles that are inserted into the placenta. Amniocentesis can be done from about 14 weeks up to about 20 weeks of the pregnancy and CVS can be done earlier, between 9.5 and 12.5 weeks, but is slightly more risky to the unborn child.

During Amniocentesis a small amount of amniotic fluid, which contains fetal tissues, is extracted from the amnion or amniotic sac surrounding a developing fetus, and the fetal DNA is examined for genetic abnormalities. Amniocentesis is not performed for every pregnancy, but is generally done when an increased risk of genetic defects in the fetus is indicated, by mother’s age (over 35 years is common), family history of genetic defects, or other factors.

Chorionic villus sampling (CVS) involves removing a sample of the chorionic villus (placental tissue) and testing it. It is generally carried out only on pregnant women over the age of 35 and those whose offspring have a higher risk of Down syndrome and other chromosomal conditions. The advantage of CVS is that it can be carried out 10-12 weeks after the last period, earlier than amniocentesis.

DNA from the developing baby may be isolated from either an amniocentesis or CVS. A karyotype may be created from fetal chromosomes following either procedure, or a specific mutation may be analyzed. The analysis of specific mutations will be discussed in the chapter titled Biotechnology.

Gene Therapy

So, how do you treat genetic disorders? If medically possible, each manifestation can be treated separately. But is there a way to use genetics to treat the root cause of the disease – that is, to fix the mistake in the DNA?

Gene therapy is the insertion of a new gene into an individual’s cells and tissues to treat a disease, replacing a mutant disease-causing allele with a normal, non-mutant allele. Although the technology is still in its early stages of development, it has been used with some success.

There are a number of mechanisms used to replace or repair a defective gene in gene therapy.

- A normal gene may be inserted into a nonspecific location within the genome to replace a nonfunctional gene. This approach is most common.
- An abnormal gene could be replaced by a normal gene through homologous recombination.
- The abnormal gene could be repaired through selective reverse mutation, which returns the gene to its normal, non-mutant state.
- The regulation (the degree to which a gene is turned on or off) of a particular gene could be altered.

As stated above, the most common gene therapy approach is to replace a disease-causing allele with a normal allele. To deliver the new allele to the appropriate cells, a carrier, called a vector, must be used. Currently, the most common type of vectors are viruses that have been genetically altered to carry normal human DNA, and not to result in any phenotypes associated with the virus. As viruses have evolved a robust method of delivering their viral genes to human cells, scientists have tried to develop (and are continuing to develop) methods to take advantage of this process, and have these vectors insert human DNA into target cells. Scientists have manipulated the viral genome to remove disease-causing genes and insert therapeutic human genes (**Figure** 8.15). For obvious reasons, this is currently a field of intense biomedical research.

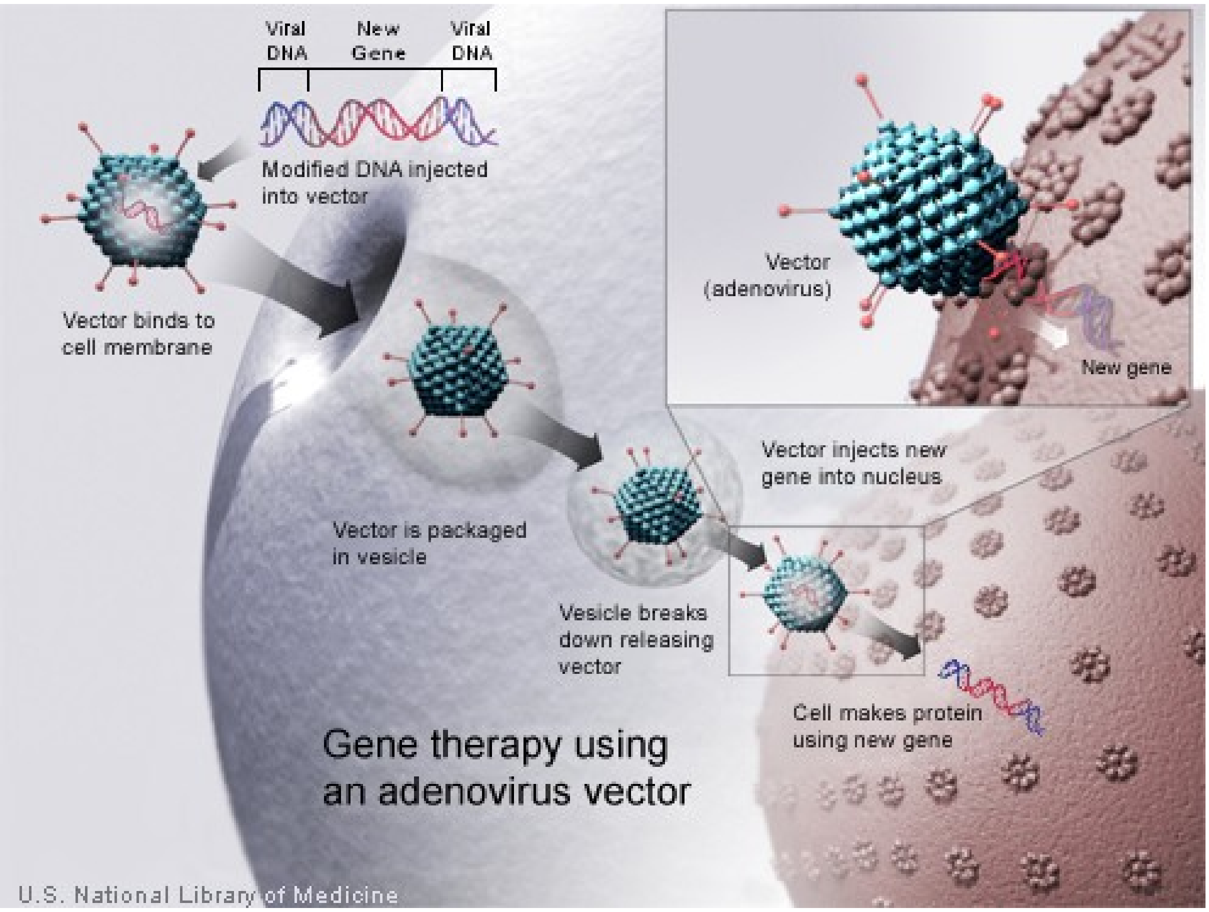

Viral DNA
New Gene
Viral DNA
Modified DNA injected into vector
Vector binds to cell membrane
Vector (adenovirus)
New gene
Vector injects new gene into nucleus
Vector is packaged in vesicle
Vesicle breaks down releasing vector
Cell makes protein using new gene
Gene therapy using an adenovirus vector
U.S. National Library of Medicine

Figure 8.15: Gene Therapy using a viral vector. The new gene is inserted into the viral genome, the virus binds to the cell membrane and enters the cell by endocytosis. The viral genome, containing the new gene is injected into the cell nucleus, where the viral DNA is transcribed, starting the process of protein synthesis.

A patient's target cells, such as liver or lung cells are infected with the genetically altered virus. The vector then unloads its genetic material containing the therapeutic human gene into the target cell. The generation of a functional protein product from the therapeutic gene should restore the target cell to a normally functioning phenotype. To date, this process has had limited success, but who can say what will happen in the future.

Severe Combined Immunodeficiency

Severe Combined Immunodeficiency, or SCID, is a heritable immunodeficiency - a genetic disorder that cripples the immune system. It is also known as the ‘bubble boy’ disease, named after David Vetter, SCID’s most famous patient who lived for over 12 years in a sterilized environment, just like living inside a “bubble.” SCID affects about 1 in 100,000 live births. These babies, if untreated, usually die within one year due to severe, recurrent infections. Treatment options have improved considerably and include bone marrow transplants and gene therapy. Children no longer have to live inside a bubble as did David Vetter, who was placed inside his sterile bubble about 10 seconds after birth. He died 15 days after he left his sterile environment, due to an undetected virus in the bone marrow transplant. David was one of the first bone marrow recipients.

More recently gene therapy has proved successful in treating SCID. Insertion of the correct gene into cells of the immune system should correct the problem. Trials started in 1990, and in 1999, the first SCID patients were detected with functional immune systems. Due to some complications these trials had to be stopped, but these issues seem to have been resolved. Gene therapy in individuals with SCID have been human genetics only gene therapy success stories. Since 1999, gene therapy has restored the immune systems of at least seventeen children with the disorder. This raises great hope for other genetic disorders. In your lifetime, it is definitely possible that many genetic disorders may be “cured” by gene therapy. As was mentioned earlier, no one can say what will happen in the future, and no one knows what lies ahead.

Epigenetics: Your ancestors can reset genes

Learn all about it:

http://learn.genetics.utah.edu/content/epigenetics/

Why your DNA isn’t your Destiny: http://www.time.com/time/health/article/0,8599,1951968,00.html

Lesson Summary

- In humans, whereas many genetic disorders are inherited in a recessive manner, simple dominant inheritance accounts for many of a person’s physical characteristics.
- Genetic diseases may also be dominantly inherited, such as with achondroplasia.
- Genetic diseases may be due to specific mutations within a gene or to large chromosomal abnormalities.
- Traits controlled by genes located on the sex chromosomes (X and Y) are called sex-linked traits.
- Any recessive allele on the X chromosome of a male will not be masked by a dominant allele.
- Codominance is when two alleles are both expressed in the heterozygous individual.
- Incomplete dominance is seen in heterozygous individuals with an intermediate phenotype.
- Traits controlled by more than two alleles have multiple alleles.
- Many genes have multiple phenotypic effects, a property called pleiotropy.
- Epistasis is when a gene at one location (locus) alters the phenotypic expression of a gene at another locus.
- Polygenic traits are due to the actions of more than one gene and often, their interaction with the environment.
- Trisomy is a state where humans have an extra autosome; they have three of a particular chromosome instead of two.
- The most common trisomy in viable births is Trisomy 21 (Down Syndrome).
- Prenatal diagnosis refers to the diagnosis of a disease or condition before the baby is born.
- Amniocentesis and choronic villus sampling are invasive methods involved in prenatal diagnosis.

- Gene therapy is the insertion of a new gene into an individual's cells and tissues to treat a disease, replacing a mutant disease-causing allele with a normal, non-mutant allele.

Review Questions

1. What is a genetic disease?
2. Discuss the main difference between autosomal and sex-linked.
3. Why is variation within the human genome important?
4. Why is it more common for males to have X-linked disorders?
5. Describe how a mutation can lead to a genetic disease.
6. Discuss how a new mutation can become a new dominant allele.
7. How are autosomal traits usually inherited? Give examples of traits.
8. How are genetic diseases usually inherited? Are there exceptions? Give examples.
9. Discuss the difference between codominance and incomplete dominance. Give examples.
10. What is meant by trisomy? **(Beginning)** How can trisomy phenotypes be detected?
11. What is the most common viable trisomy disorder?
12. List conditions involving an abnormal number of sex chromosomes.
13. Why is genetic counseling important?
14. What is gene therapy?
15. Describe the most common approach to gene therapy.

Further Reading / Supplemental Links

- The National Human Genome research Institute:
- http://www.genome.gov
- The Dolan DNA Learning Center:
- http://www.dnalc.org/home_alternate.html
- DNA Interactive:
- http://www.dnai.org/
- A Science Odyssey: DNA Workshop:
- http://www.pbs.org/wgbh/aso/tryit/dna/
- Kimball's Biology Pages:
- http://users.rcn.com/jkimball.ma.ultranet/BiologyPages
- http://en.wikipedia.org

Vocabulary

achondroplasia An autosomal dominant disorder; the most common cause of dwarfism.

amniocentesis A prenatal diagnostic procedure in which a small amount of amniotic fluid, which contains fetal tissues, is extracted from the amnion or amniotic sac surrounding a developing fetus, so that the fetal DNA is examined for genetic abnormalities.

autosomal dominant disorder A disorder in which only one mutated allele is needed for a person to be affected.

autosomal recessive disorder A disorder in which both copies of the gene must be mutated for a person to be affected.

autosome Any chromosome other than a sex chromosome.

chorionic villus sampling (CVS) A prenatal diagnostic procedure which involves removing a sample of the chorionic villus (placental tissue) and testing it.

codominance When two alleles are both expressed in the heterozygous individual; both alleles affect the phenotype in separate and distinguishable ways.

cystic fibrosis (CF) A recessive inheritable disorder caused by a mutation in a gene called the cystic fibrosis transmembrane conductance regulator (CFTR).

Duchenne muscular dystrophy (DMD) The most common type of muscular dystrophy; an X-linked recessive disorder.

epistasis When a gene at one location (locus) alters the phenotypic expression of a gene at another locus.

gene therapy The insertion of a new gene into an individual's cells and tissues to treat a disease, replacing a mutant disease-causing allele with a normal, non-mutant allele.

genetic counseling The process by which individuals or their families who are at risk of an inherited disorder are counseled on many different aspects of the disorder.

genetic counselor An individual trained in human genetics and counseling.

hemophilia A group of diseases in which blood does not clot normally.

incomplete dominance Occurs in heterozygous individuals with an intermediate phenotype; neither allele is dominant over the other.

Klinefelter's syndrome Caused by the presence of one or more extra copies of the X chromosome in a male's cells.

multiple allele traits Traits controlled by more than two alleles.

muscular dystrophy A term encompassing a variety of muscle wasting diseases.

mutation A change in the nucleotide sequence of DNA or RNA.

nondisjunction The failure of replicated chromosomes to separate during anaphase II of meiosis.

pedigree A chart which shows all of the known individuals within a family with a particular phenotype; a representation of genetic inheritance.

Phenylketonuria (PKU) An autosomal recessive genetic disorder characterized the inability to metabolize the amino acid phenylalanine.

pleiotropy Having multiple phenotypic effects.

polygenic traits Traits that are due to the actions of more than one gene and often, their interaction with the environment.

prenatal diagnosis The diagnosis of a disease or condition in a developing baby; done before the baby is born.

Severe Combined Immunodeficiency (SCID) A heritable immunodeficiency; a genetic disorder that cripples the immune system.

sex chromosomes Specify an organism's genetic sex; in humans, the X and Y chromosomes.

sex-linked traits Traits controlled by genes located on the sex chromosomes (X and Y).

Tay-Sachs disease An autosomal recessive genetic disorder that is fatal in early childhood; results from the accumulation of harmful quantities of fat in the nerve cells of the brain.

trisomy A state where humans have an extra autosome, having 47 chromosomes instead of 46. For example, trisomy 16 results in a third chromosome 16.

trisomy 21 Down syndrome; individuals often have some degree of mental retardation, some impairment of physical growth, and a specific facial appearance.

trisomy X Triple X syndrome; results from an extra copy of the X chromosome in each of a female's cells.

X-linked disorder A disorder caused by a mutation in a gene on the X chromosome; may be dominant or recessive, though the majority of X-linked disorders are recessive.

Y-linked disorder A disorder caused by a mutation in a gene on the Y chromosome; only affects males.

Points to Consider

In this chapter, we discussed human genetics as involved in human health. In the next chapter, we will discuss biotechnology. With gene therapy, we can see how biotechnology will play a significant role in society's future.

- Can you speculate on the role of biotechnology in our future?
- What other roles for biotechnology do you envision?
- Why is biotechnology important?